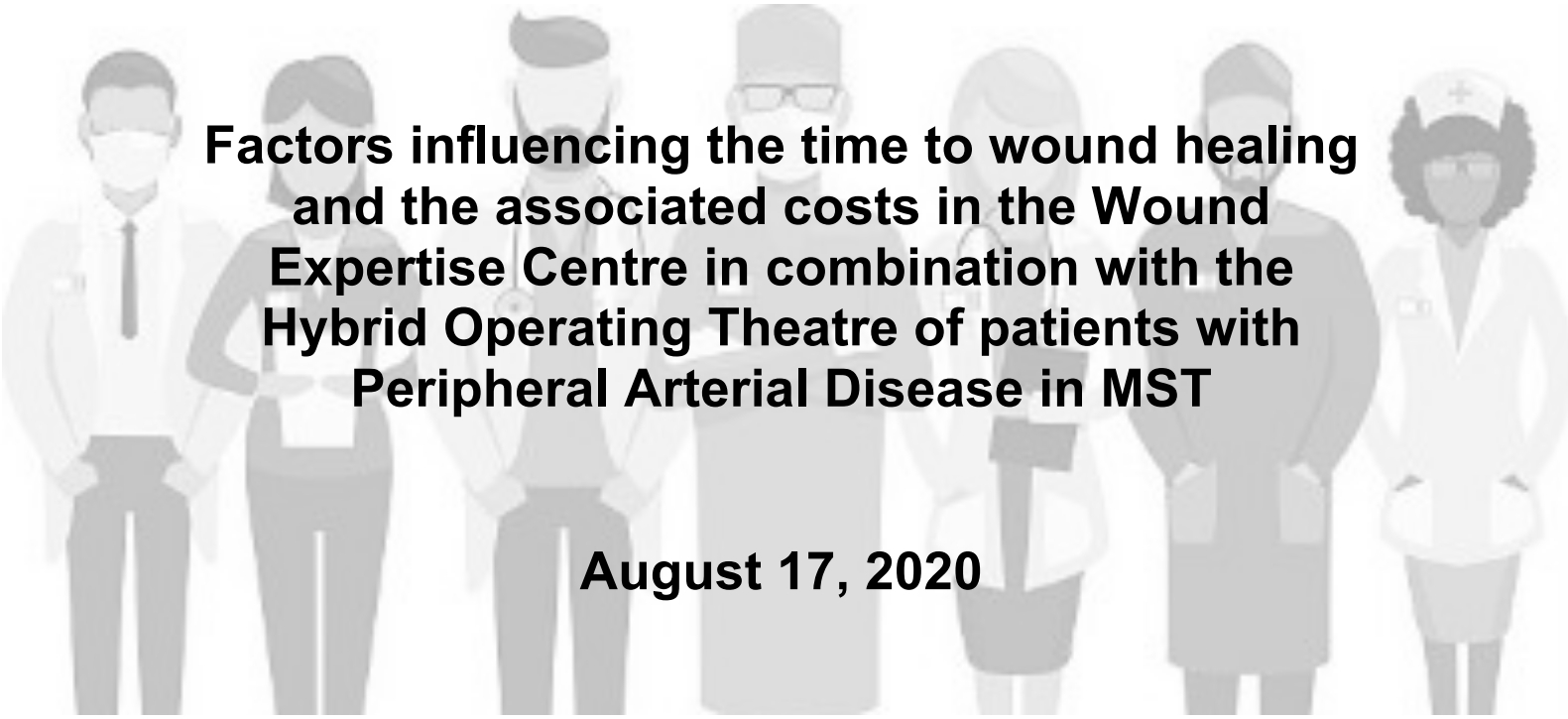

Factors influencing the time to wound healing and the associated costs in the Wound Expertise Centre in combination with the Hybrid Operating Theatre of patients with Peripheral Arterial Disease in MST

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Preface

In front of you lies the thesis ‘Factors influencing the time to wound healing and the associated costs in the Wound Expertise Centre in combination with the Hybrid Operating Theatre of patients with Peripheral Arterial Disease in MST’. The thesis is written as part of my graduation from the Health Sciences study program at the University of Twente and on behalf of the Surgical department of Medisch Spectrum Twente (MST). The study was conducted from February 2020 up to August 2020 and contributes to the optimization of the treatment process in the Wound Expertise Centre in combination with the Hybrid Operating Theatre.

I have learned a lot by doing my master thesis. From collecting all the data by myself to coming up with a final advice. During the process, I experienced some ups and downs. Due to COVID-19 the process did not really turn out to be as expected. However, the ups and downs helped me to develop my skills focused on quantitative data analysis and professional behavior.

I am very thankful I got the opportunity to conduct my research for MST. Firstly I would like to thank my external supervisor, Dr. R. Meerwaldt for being the source of inspiration behind the study. Secondly, Prof. Dr. B. Geelkerken for his help especially with the medical part of the research and critical feedback. Thirdly, Dr. B.Wermelink for the critical feedback. I would also like to thank my second supervisors Dr. Erik Koffijberg and Drs. X. Pouwels for the help with the analyses.

I hope you will enjoy reading this paper.

Isabelle Hey
Enschede, 17th of August 2020.

Abstract

Background: Each year, 500,000 patients in the Netherlands develop complex wounds, leading to an estimated cost of €3.2 billion for wound care. Complex wounds include diabetic ulcers, arterial ulcers, pressure ulcers, burns and traumatic ulcers. One of the main causes for the development of complex wounds is PAOD. Chronic obstructive vascular disease can be further divided into intermittent claudication and critical ischemia. The prevalence of chronic obstructive vascular disease is 7% of people over the age of 55 and 56% of people over the age of 85 years. The prevalence of critical ischemia is 0.5–1%. The costs with regard to wound care is expected to rise because of aging and the increasing prevalence of chronic diseases. In order to maintain these costs and the quality of care, WECs and HOTs have been founded since a few years. Studies regarding the treatment process and outcomes of patients with PAOD, treated in the WEC in combination with the HOT are scarce. The primary outcome parameter of wound care in the WEC and HOT is the time to wound healing. Previous studies that mentioned the time to wound healing for patients with PAOD mainly focused on wound healing within six months. Findings of this study can significantly contribute to a shorter time to wound healing which can make a difference in patient's lives and the costs of caring for patients with complex wounds and PAOD in the WEC and HOT.

Objective: To determine which factors influence the time to wound healing and the associated cost for patients with PAOD, receiving wound care in the WEC and a revascularisation procedure in the HOT.

Method: Patients with PAOD who entered the WEC with tissue loss (Rutherford classification 5/6) and received an intervention in the HOT were included retrospectively over a period between 2017 and 2019. Outcome measures were; time to wound healing, the proportion of patients with healed wounds within six months, factors influencing wound healing within six months and the costs related to the time to wound healing were analysed.

Results: A total of 135 patients were included in the study. Complete wound healing was achieved in 90 (66.7%) patients, whereof 40 (44,4%) of the patients experienced wound healing within six months. Diabetic foot (OR= 0,366), time between admission WEC and the surgery in the HOT (OR= 0,909) and the occurrence of complications (OR= 0,219) were factors that resulted in a lower probability of wound healing within six months. The total average costs per patient did not differ between patients who experienced wound healing within six months and patients who did not. The average total costs were higher when patients had either an major amputation (€14.584 SD= 9,690) or not (€11.041 SD= 7,481), complication (€16.001 SD= 8,534) or not (€9.703 SD= 7,499) or redo surgery (€19.003 SD= 7,382) or not (€9.467 SD= 4,569).

Conclusion: Factors that influence the time to wound healing within six months are having a Diabetic foot, time between admission in the WEC and the decision for treatment in the HOT and the occurrence of complications. Besides, major amputation, occurrence of complications and the number of surgeries are associated with higher costs.

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List of Acronyms

ABI = Ankle-Brachial Index
AUC = Area Under the Curve
BMI= Body Mass Index
CT= Computed Tomography
CTA= Computed Tomography Angiography
CVA = Cerebrovascular Accident
DM = Diabetes Mellitus
EVT = Endovascular Treatment
DBC = Diagnose Behandel Combinatie
GP = General Practitioner
HOT = Hybrid Operating Theatre
ITN= Intrathecal Narcotics
MDO = Multidisciplinary Meeting
MRA= Magnetic Resonance Angiography
MRI= Magnetic Resonance Imaging
MST= Medisch Spectrum Twente
OR = Odds Ratio
PTA = Percutaneous Transluminal Angiography
PAOD = Peripheral Arterial Occlusive Disease
R4 = Rutherford classification 4
R5 = Rutherford classification 5
R6 = Rutherford classification 6
ROC = Receiver Operating Curve
SD = Standard Deviation
TIA = Transient Ischemic Attack
WEC = Wound Expertise Centre
WIFI = Wound, Ischemia and Foot Infection

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1. Introduction

Peripheral Arterial Occlusive Disease

Each year, 500,000 patients in the Netherlands develop complex wounds [1], leading to an estimated cost of €3.2 billion for wound care. Complex wounds include diabetic ulcers, arterial ulcers, pressure ulcers, burns and traumatic ulcers. One of the main causes for the development of complex wounds is peripheral arterial occlusive disease (PAOD). PAOD is a clinical manifestation of cardiovascular disease caused by atherothrombosis, which can be divided into chronic obstructive vascular disease and acute ischemia. Chronic obstructive vascular disease can be further divided into intermittent claudication and critical ischemia [2]. The prevalence of chronic obstructive vascular disease is 7% of people over the age of 55 and 56% of people over the age of 85 years [2]. The prevalence of critical ischemia is 0.5–1% [2].

Patients with PAOD are classified according to the Rutherford or Fontaine classification [2]. These classifications range from asymptomatic to major tissue loss. In 2017, €956 million was spent on treating PAOD in the Netherlands [3]. Out of this amount, 75.3% was spent on the elderly patients, 65 years and older [4]. Several risk factors are associated with the development of PAOD. The major risk factors associated with PAOD are gender, diabetes mellitus (DM), hypertension, smoking, hyperlipidaemia, metabolic syndrome, and a history of cardiovascular events [5-13]. In addition, older people are more likely to develop PAOD. However, PAOD also manifests at a younger age in men [7]. In patients with PAOD, DM is associated with higher rates of mortality (29%) and amputation (14 to 24%) [9;14].

PAOD is currently treated with lifestyle changes, medication such as blood pressure lowering medicines, wound care, or a revascularisation procedure. Revascularisation procedures include percutaneous transluminal angioplasty (PTA), PTA and stent, endarterectomy, autogenous or prosthetic bypass surgery [15]. Wound care has been fragmented among specialists and practitioners both inside and outside hospitals. In recent years, wound care treatment has become increasingly centralised to manage care more efficiently.

Wound Expertise Centre

The cost of wound care is expected to rise due to the aging of the general population combined with an increase in the prevalence of chronic diseases [16]. To prevent rapid increases in wound care cost while maintaining high quality of care, wound expertise centres (WECs) have been established in recent years. In these centres, various specialists work together in a multidisciplinary approach. The focus of the treatment is not only on the underlying pathology but also on reconstructive and prosthetic therapies. Consequently, patients with complex wounds receive more efficient treatment and better quality of care [17-24]. MST (Medisch Spectrum Twente) established a WEC in 2016 [17], where surgeons, dermatologists, rehabilitation physicians, and plastic surgeons combine their expertise. Referrals to the WEC come from general practitioners, geriatric specialists, and departments in MST. Complex and acute wounds that do not exhibit a tendency to heal within two weeks are treated in MST's WEC.

Before the existence of WECs, communication regarding wound care among all associated caregivers was limited [18] and the treatment fragmented and, therefore, often inefficient. It can be concluded from the literature that WECs ensure cost savings and improved wound healing rates [19-24], with an average cost saving of between €1.280 and €2.533 per patient. A study by Moffat et al. showed an increase in the rate of healing from 22% to 67% in a 12-week period [22]. This increased wound healing rate resulted in fewer amputations [23]. The savings can be attributed to the treatment, treatment duration, and outcomes [20]. The cost saving can be explained by the following aspects: 1) fewer referrals to medical specialists because patients are referred to the WEC [20]; 2) shorter time for wound healing leads to less demand for treatment and use of bandages [20]; and 3) the wound healing rate is higher, which resulted in cost savings

for hospital care, pharmacy, geriatric rehabilitation care, and nursing [20]. Treatment policies are discussed by various specialists, with differing expertise, to ensure that patients receive personalised treatment. Surgical options for treatment are revascularisations, which are mainly performed in the Hybrid Operating Theatre (HOT).

Hybrid Operating Theatre

In 2016, MST established a HOT [25], in which a conventional operating theatre and advanced X-ray room are combined. In the HOT, high-quality imaging techniques are used to provide improved support during procedures. The HOT makes it possible to perform hybrid procedures that combine the benefits of open and endovascular surgery during the same procedure. It can be concluded from several studies [26-32] that endovascular treatments (EVT) are less demanding for patients, are associated with fewer complications, less chance of infections, and faster recovery. The effectiveness of the HOT depends on a combination of factors, focusing on the surgery, the expertise of the surgeons, the teamwork in the HOT, and communication before, during and after surgery among healthcare providers [33].

Current Treatment

An overview of the current treatment process for PAOD patients admitted to the WEC and requiring surgery in the HOT is shown in Figure 1. Patients might need an amputation if revascularisation is no longer an option. There is also a possibility that patients might require redo surgery if the wound does not heal after the first surgery. An amputation or redo surgery can result in a longer time to wound healing [34-35].

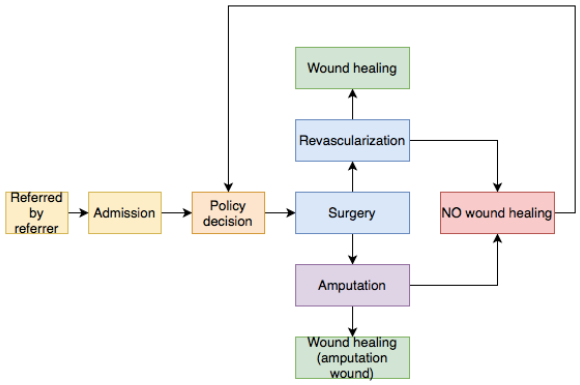

Figure 1 Overview of follow up process for the treatment combination in the WEC and HOT for patients with PAOD (referrer= General Practitioner, Geriatric specialist or departments in MST)

Wound Healing Factors

Time to wound healing is an important outcome parameter for patients suffering from PAOD. Several studies have focused on factors associated with wound healing duration [36-42]. Most studies observed wound healing rates within six months (Table 1). The differences in time to wound healing are mainly due to the type of wound and the presence of infections [39;41]. Diabetic foot ulcers associated with PAOD take a longer time to heal as compared to arterial ulcers.

Table 1 Time to wound healing per study

Kind of ulcer(s)	DM (%)	Smoking (%)	Age (Mean)	Time to wound healing	Study population
PAOD ulcers	66%	51%	68	6 months 42%, 12 months 75%	334 patients [36]
PAOD ulcers	81%	X	67	6 months 72.2%, 12 months 86.9%	249 patients [37]
PAOD ulcers				6 months:	177 patients [38]
	71%	42%	73	Toe ulcers 64%	
	82%	29%	73	Heel ulcer 36%	
	78%	43%	71	Extensive ulcers on fore foot 5%	
PAOD leg ulcers	50%	X	76	6 months; 40%, 12 months; 75%	150 patients [40]
PAOD ulcers	66.7%	53.3%	75.5	6 months: 56.3%	97 patients [42]

It can be concluded from the previous studies that the factors DM, Rutherford classification 6, ulcer location, cardiovascular disease, age, obesity, smoking, malnutrition, and alcohol abuse negatively influence time to wound healing [36-43]. Obese patients are at risk of various diseases, such as coronary heart diseases, DM type 2, cancer, hypertension, stroke, and respiratory problems. These diseases can cause a delay in time to wound healing because of the probability of wound complications. Ageing is a risk factor for impaired wound healing due to an altered inflammatory response [44-45]. Lastly, smoking is a factor that delays the time to wound healing. Smoking results in an increasing risk of heart and vascular diseases, stroke, chronic lung disease, and cancer. Smoking causes complications, such as infections and wound rupture. Complications that occur during or after surgery are classified according the Clavien-Dindo classification.

Clavien-Dindo Classification

The Clavien-Dindo classification is a quality assessment tool that documents postoperative complications based on the therapy used to treat these complications. This tool makes it possible to compare surgical results among different surgeons and therapies. Insights from the Clavien-Dindo classification into the treatment of complications made it possible to respond more effectively to complications and have resulted in a reduction in treatment costs and improved quality of treatment. The Clavien-Dindo classification tool consists of five grades, from no deviation of the normal course to the death of the patient. Several studies concluded that the classification of complications is correlated with the length of hospital stay and the complexity of the primary surgery [46-47].

Aim of the Study

There is evidence available in the literature regarding the processes and outcomes of the WEC and the HOT surgeries individually. Unfortunately, limited information is available regarding the process and outcomes of the treatment combination of the WEC and HOT interventions, specifically for patients with PAOD. An important outcome of the treatment combination is time to wound healing. In this study, insight was gained into the current treatment combination, focussing on time to wound healing up to a period of six months. Wound healing within six months was selected to enable comparison of the results of this study with those of previous studies. Insight into the effectiveness and cost of the treatment combination of the WEC and HOT will enable recommendations for improving the efficiency of the WEC and HOT. Findings of this study can significantly contribute to a shorter time to wound healing which can make a difference in patient's lives and the costs of caring for patients with complex wounds and PAOD. Therefore, the following research question was formulated:

Which factors influenced the time to wound healing and the cost for patients with PAOD who received wound care in the WEC and underwent an intervention in the HOT of MST?

Sub-questions that were formulated to answer the research question are:

- What is the current time to wound healing in patients with PAOD in the WEC in combination with interventions in the HOT?
- What factors are associated with the time to wound healing within six months in patients with PAOD?
- What are the costs associated with the current time to wound healing in patients with PAOD in the WEC and the HOT?

Chapter 1 contains the introduction and sets out the relevance and aim of the study. In Chapter 2 the methods employed in this study are discussed, including the study population, data collection and the methods used to analyze the three sub questions. Chapter 3 showed the socio-demographics of the patients included in the study and the results regarding the three sub questions. Chapter 4 showed the discussion per sub question, the limitations and the recommendations. Chapter 5 gives the answer to the research question.

2. Methods

This chapter discusses the study design, study population, data collection, and data analysis.

2.1 Study Design

To answer the research question and sub questions a retrospective study was set up where data was analysed quantitively. The study was performed between February and July 2020. The data was collected from the databases of the MST for the time period between 2017-2019.

To answer the first sub-question, *'What is the current time to wound healing in patients with PAOD in the WEC in combination with the HOT?',* a quantitative study that included two steps was conducted. These steps provided insights into the current time to wound healing in patients with PAOD who were treated in the WEC and HOT of MST. The first step was to create a timeline that showed the amount of time spent on each procedure in the wound healing process. Secondly, bar charts were created to show the differences among the patients regarding the time to wound healing.

The second sub-question 'What factors are associated with the time to wound healing within six months in patients with PAOD?' was answered through the use of a quantitative study. To determine which factors were of importance for the time to wound healing within six months, a logistic regression model was applied. Factors used for the logistic regression model were based on expert opinions, univariate analyses, and the literature. Expert opinions were collected through the use of a survey. Experts could indicate the factors they believe played an important role in the time to wound healing in the survey.

The third sub-question *'What are the costs associated with the current wound care in the WEC and the HOT in patients with PAOD?'* was answered through the use of a quantitative study and provided insights into the costs related to the time to wound healing. Bar and pie charts were created to clearly depict the differences in costs among patients.

2.2 Study Population

Patients included in the study were treated in the WEC between 2017–2019 (Table 2). Data was collected from the databases between March 2020 and May 2020.

Table 2 Inclusion and exclusion criteria

	Inclusion criteria		Exclusion criteria
1	Patients classified with Rutherford Classification 4-6 (critical limb ischemia)	1	Patients classified with Rutherford Classification 0-3 (Acute ischemia and intermittent claudication)
2	Patients with complex wound (s)	2	Patients without complex wounds
3	Patients with diabetic, arterial, or traumatic ulcers	3	Patients with burns or decubitus ulcers
4	Patients referred to the WEC	4	Patients not referred to the WEC
5	Patients who have had consults in the WEC	5	Patients who have had no consults in the WEC
6	Patients who received surgical treatment in the HOT	6	Patients who had not had surgical treatment in the HOT
7	Patients who did not die during the follow-up period in the WEC.	7	Patients who died during the follow-up period in the WEC
8	Patients who started treatment between 2017–2019	8	Patients who started treatment in the WEC before 2017
9	Patients who experienced wound healing between 2017 – May 2020	9	Patients who started treatment in the WEC after 2019
10	Patients treated only in the MST during the time to wound healing	11	Patients treated in another hospital during the time to wound healing
		12	Patients whose treatment focused on comorbidities

Rutherford classification 4 (R4) was used for inclusion because the Rutherford classification and the Fontaine classification are used but are sometimes being used interchangeable. The R4 does not classify patients with wounds in daily practice. Patients with traumatic ulcer and diabetic ulcers were only included in the study if the underlying diagnosis was PAOD. Patients who died before wound healing was achieved were excluded from the study because wound healing was not achieved. In addition, those patients died due to the presence of comorbidities. Patients whose treatment focused on comorbidities were excluded from the study due to the difficulty in tracing consults only intended for complex wounds rather than comorbidities. Moreover, not all consults for these patients were done in the WEC.

2.3 Data Collection

Data was collected from the vascular registration databases of MST between 2017–2019. Corresponding patient files were consulted to collect information regarding patient, procedure, and surgery characteristics. This data was collected using the software programs Xcare, ORsuite, and DSV. Patient data was coded with an identification number. The coded identification number consisted of two letters and three digits, such as MS001. The letters indicated the data from MST, and the digits were assigned randomly. These codes were not traceable to the specific patients, and the key to the codes was protected by the principle investigator.

In total, 161 variables were collected per patient using Microsoft Excel (Appendix A). Continuous variables were displayed as a mean combined with the standard deviation (SD). Categorial variables were displayed as quantities together with the corresponding percentage (Appendix B). The variable BMI was divided in the categories: 1) underweight (BMI < 18.5), 2) normal weight (BMI 18.5–25) 3), overweight (BMI 25–30), and 4) obese (BMI > 30). The risk factors, smoking, cardiac risk, cerebrovascular risk, DM, and hyperlipidaemia were divided into two categories, (0) no and (1) yes. The following variables were combined or disaggregated as follows:

- ‘Date Referral’ + ‘Date first consult’ = ‘TimeFromReferralToFirstConsult’
- ‘Vascular surgeon at admission’ + ‘Nurse at admission’ + ‘Podiatrist at admission’ + ‘Physiatrist at admission’ + ‘other at admission’ = ‘Specialist(s)AtAdmission’
- ‘MRA’ + ‘CTA’ + ‘Duplex’ + ‘MRI’ + ‘CT’ + ‘X-ray’ + ‘Other’ = ‘AdditionalExamination’
- ‘Date first consult’ + ‘Date operation’ = ‘TotalTimeUntilExecutingOperation’
- ‘Date first consult’ + ‘Date determining policy’ = ‘TimeBetweenadmissionWECANDDecisionTreatmentHOT’
- ‘Date determining policy’ + ‘Date operation’ = ‘TimeBetweenDecisionTreatmentHOTANDSurgeryHOT’
- ‘OperationType’ = ‘SurgeryLocation’ + ‘SurgeryOpen’ + ‘SurgeryAdditional’
- ‘Start time operation’ + ‘End time operation’ = ‘OperationTime’
- ‘Lengths of hospital stay 1’ + ‘Lengths of hospital stay 2’ + ‘Lengths of hospital stay 3’ ‘Lengths of hospital stay 4’ = ‘TotalLengthsOfHospitalStay’

The variable ‘TimeFromReferralToFirstConsult’ represented the time between referral and admission to the WEC. For the variable ‘TotalLengthsOfHospitalStay’ the hospital stays, pre- and postoperative admission, for every surgery were added together.

The variable ‘Earlier return’ represented the number of times a patient returned before previously planned consults. Earlier returns could result from aggravated pain, complaints, or infections. The time between development of the wound until the admission consult in the WEC was represented by the variable ‘wound existence’. The variable ‘referral by’ represented the type of caregiver who referred the patient to the WEC. The variable ‘additional examination’ included MRA (Magnetic Resonance Angiography), CTA (Computed Tomography Angiography), duplex ultrasound, or x-ray photographs. The variables ‘amputation risk’ and ‘revascularisation benefit’ represented the WIFI score and reflected the complexity, infection severity, and degree of perfusion. The WIFI score is classified in four stages from stage 1, which represents low complexity, low infection severity, and high degree of perfusion, to stage 4, which represents high complexity, high infection severity, and low degree of perfusion. The variable ‘operation type’ was divided into the location of the surgery, open surgery, and additional surgery. This resulted in better insight into the complexity of the operations.

The costs regarding the time to wound healing were collected using the software programmes Business Objects and Xcare. A database was set up for the specific costs with the business controller and the DBC (Diagnose Behandel Combinatie) Controller of the MST. The database contained the prices per procedure, categorised for each year between and including 2017-2020. Prices for consults with podiatrists were not in the database and were collected from the podiatrists linked to MST and the ‘cost manual for economic evaluations’ of the Zorginstituut Nederland (ZIN) [48]. In addition, the hourly wages for specialists, assistants, and the prices per type of anaesthesia were included in the average price of a surgery. MST set an average price for a specific surgery at the beginning of the year. Table 3 shows the average prices per annum. The average prices during 2017–2020 were calculated and used to obtain representative input because the amounts differed over the years. The average price per gypsum consultation was €93.27. This was calculated without taking into account the duration of the gypsum consults.

Table 3 Prices of time to wound healing process

VARIABLE	CODE	2017	2018	2019	2020	AVERAGE
ADMISSION CONSULT	190060	€ 201.31	€ 197.01	€ 200.86	€ 198.61	€ 199,45
CONTROL CONSULT	190013	€ 85.80	€ 87.70	€ 90.57	€ 95.04	€ 89,78
CONSULTCODE OC (OTHER CONSULTS)	ZOC	€ 13.53	€ 13.86	€ 15.46	€ 14.04	€ 14,22
CONTROL CONSULT		€ 49.67	€ 50.78	€ 53.01	€ 54.54	€ 52,00
PHONE CONSULT	ZTELC	€ 52.91	€ 33.72	€ 35.50	€ 35.45	€ 39,40
GYPSUM CONSULT 10 MIN	ZGB10	€ 33.18	€ 35.12	€ 36.31	€ 36.92	€ 35,38
GYPSUM CONSULT 20 MIN	ZGB20	€ 57.19	€ 61.45	€ 63.54	€ 64.61	€ 61,70
GYPSUM CONSULT 30 MIN	ZGB30	€ 82.98	€ 87.87	€ 90.77	€ 92.27	€ 88,47
GYPSUM CONSULT 40 MIN	ZGB40	€ 110.83	€ 114.12	€ 118.11	€ 119.95	€ 115,75
GYPSUM CONSULT 60 MIN	ZGB60	€ 145.62	€ 166.70	€ 172.56	€ 175.24	€ 165,03
OTHER CONSULTS	ZOC	€ 13.53	€ 13.86	€ 15.46	€ 14.04	€ 14,22
SPECIALISTS AT ADMISSION						€ -
-PODIATRIST CONSULT		€ 22.00	€ 22.00	€ 22.00	€ 22.00	€ 22,00
-PARAMEDICAL CARE		€ 32.50	€ 32.50	€ 32.50	€ 32.50	€ 32,50
-PHYSIATRIST		€ 135.00	€ 135.00	€ 135.00	€ 135.00	€ 135,00
-DIETITIAN CONSULT	BTCDE 3	€ 8.77	€ 9.18	€ 11.10	€ 9.55	€ 9,65
MDO	190005	€ 50.20	€ 48.71	€ 51.98	€ 52.78	€ 50,92
ADDITIONAL EXAMINATION						€ -
- MRA		€ 201.68	€ 208.02	€ 213.85	€ 219.08	€ 210,66
- CTA		€ 155.62	€ 159.76	€ 164.79	€ 167.71	€ 161,97
- ECHO	89070	€ 65.56	€ 67.51	€ 69.56	€ 70.67	€ 68,32
- DUPLEX	39775	€ 17.45	€ 17.93	€ 18.48	€ 18.81	€ 18,17
- MRI	89090	€ 136.83	€ 141.47	€ 145.15	€ 149.19	€ 143,16
- CT	89142	€ 90.76	€ 93.21	€ 96.08	€ 97.82	€ 94,47
- X-RAY		€ 60.72	€ 62.41	€ 64.44	€ 65.52	€ 63,27
RADIOLOGICAL RESEARCH THORAX, ONE OR MORE DIRECTIONS	85002	€ 61.79	€ 63.62	€ 65.58	€ 66.69	€ 64,42
RADIOLOGICAL EXAMINATION ONLY AND/OR FOOT (ROOT) AND/OR TOES.	89602	€ 59.65	€ 61.20	€ 63.30	€ 64.35	€ 62,13
CONTRAST FLUID	Z26687	€ 64.85	€ 66.55	€ 68.70	€ 69.90	€ 67,50
HOSPITAL STAY	190218	€ 502.85	€ 519.19	€ 521.35	€ 315.96	€ 464,84
AMPUTATION TARSUS OF A TOE	038790	€ 938.42	€ 959.35	€ 505.00		€ 800,92
AMPUTATION TOE	038791	€ 1,867.49	€ 1,909.61	€ 1,961.17	€ 2,117.13	€ 1,963,85
AMPUTATION LOWER LEG	038690	€ 1,862.34	€ 1,971.43	€ 1,975.67	€ 2,069.02	€ 1,969,62
AMPUTATION UPPER LEG	038590	€ 1,755.88	€ 1,808.93	€ 1,436.16	€ 1,896.20	€ 1,717,54
FEMORO-POPLITEAL BYPASS	033678	€ 3,956.24	€ 4,082.44	€ 4,201.40	€ 4,269.71	€ 4,127,45
FEMORO-TIBIAL BYPASS	033680	€ 5,003.04	€ 5,168.51	€ 5,034.52	€ 5,381.85	€ 5,146,98
CROSS OVER ARTERIA SUBCLAVIA OF ARTERIA FEMORALIS	033677	€ 3,477.05	€ 3,546.28	€ 3,678.82	€ 3,733.55	€ 3,608,93
RECONSTRUCTION PERIPHERAL ARTERY	033670	€ 3,548.64	€ 3,642.90	€ 3,760.11	€ 3,817.42	€ 3,692,27
RECONSTRUCTION PERIPHERAL ARTERY WITHOUT GRAFT	033684	€ 2,872.83	€ 2,948.71	€ 2,921.64	€ 3,091.38	€ 2,958,64
PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY – NOT CORONARY CENTRAL	033351	€ 2,084.66	€ 2,138.85	€ 2,198.53	€ 2,249.25	€ 2,167,82
PERCUTANEOUS ANGIOPLASTY – NOT CORONARY PERIPHERAL ARTERY	033672	€ 1,808.08	€ 1,860.50	€ 1,905.20	€ 1,950.59	€ 1,881,09

2.4 Data Analysis

2.4.1 Time to wound healing

The data collected for the first sub-question was analysed using Microsoft Excel. The time to wound healing was visualised on a timeline and on bar charts. The timeline represents the average time (+- SD) between each subsequent step in the treatment process and the number of patients involved in each step. The bar charts represent the total time to wound healing. Seven bar charts were created, and the first bar chart includes the total study population. The other bar charts consist of:

1) Patients with an amputation
2) Patients without an amputation
3) Patients with one surgery
4) Patients with redo surgeries.
5) Patients with complications
6) Patients without complications.

Bar charts for amputations, redo surgeries, and complications were created to obtain more insight into the differences in time to wound healing compared to patients who did not undergo an amputation, redo surgery, or had a complication. The bar charts contain seventeen variables that are shown below.

1) 'TimeFromReferralToAdmissionWEC'
2) 'TimeBetweenAdmissionWECANDDecisionTreatmentHOT1'
3) 'TimeBetweenDecisionTreatmentHOTANDSurgeryHOT1'
4) 'Amputation 1'
5) 'TimeAfterSurgery1'
6) 'TimebetweenfirstsurgeryANDDecisionTreatmentHOT2;
7) 'TimeBetweenDecisionTreatmentHOTANDSurgeryHOT2'
8) 'Amputation 2'
9) 'TimeAfterSurgery2'
10) 'TimebetweensecondsurgeryANDDecisionTreatmentHOT3'
11) 'TimeBetweenDecisionTreatmentHOTANDSurgeryHOT3'
12) 'Amputation3'
13) 'TimeAfterSurgery3'
14) ''TimebetweenthirdsurgeryANDDecisionTreatmentHOT4'
15) 'TimeBetweenDecisionTreatmentHOTANDSurgeryHOT4'
16) 'Amputation4'.
17) 'TimeAfterSurgery4'.

Variable number 2, 'TimeBetweenAdmissionANDDecisionTreatmentHOT1', represents the time between patients entering the WEC and the determination of the treatment. Variable number 3, 'TimeBetweenDecisionTreatmentHOTANDSurgery1', represents the time between the determination of the treatment policy and the first surgery. Variables number 6,10, and 14 represent the time from the completion of a surgery until the determination of a possible redo surgery. Variable 7,11, and 15 represent the time from the determination of the following surgery until executing the surgery. Variables 4, 8, 12, and 16 represent amputation. Variables 5,9,13, and 17 represent the total time in weeks after the completion of the first, second, third, or fourth surgery if a redo surgery was required.

2.4.2 Factors Related to Impaired or Improved Time to Wound Healing within six months

The second sub-question was answered through using SPSS. A logistic multivariate analysis was performed with the outcome measure 'wound healing within six months'; this was a dichotomous variable with the categories (0) no wound healing within six months and (1) wound healing within six months. P-values < 0.05 were considered significant, which indicated that there was a 5% chance that the outcome was coincidental. The number of variables used in the multivariate analysis was dependent on the number of events. At least 10 patients per variable have had to experience wound healing or not within six months to prevent overfitting. Overfitting is caused by too many variables relative to the number of observations, resulting in a complex model and misleading outcomes [49]. The variables used for the multivariate analysis were based on expert opinion, univariate analyses, and the literature. Variables associated with time to wound healing were obtained from expert opinions and previous studies. To be included in the multivariate analysis, the variables had to meet two criteria. First, the univariate analysis of the variables or the analysis of variance (ANOVA) test had to show a significance level below 0.2. Second, the variable had to appear in either the previous studies or the expert opinions. Variables that were not significant in the multivariate analysis were excluded.

Expert opinions were obtained with a short survey of four vascular surgeons, four wound specialists, and eleven surgical residents (Appendix D). In the survey, the experts had to indicate which variables, in their opinion, were associated with and had influence on the time to wound healing, and whether this was based on their own opinion or on scientific evidence. The cardiological grading system of the European Society of Cardiology was applied in this survey [48].

For the univariate analyses, a total of 46 variables were used (Appendix C). The variables belonging to the second, third, or fourth surgery were not analysed in the logistic regression analyses. These variables had no potential influence on the time to wound healing due to the fact that it is not possible to predict in advance whether a patient will require a redo surgery. The significance levels for the variables that consisted of more than two categories were acquired through the use of ANOVA or the Welch test. These tests indicated whether there were any differences among the groups. To decide whether the ANOVA test or the Welch test should be used, the Levene's test was conducted. This technique was used to check the homogeneity of the variances between the groups. If the significance level was below 0.05, the variances between the groups were not equal, which resulted in the use of the Welch test instead of the ANOVA test.

Odds ratios (OR), Nagelkerke R Square, significance levels, and the confidence interval resulted from the univariate analyses and the multivariate analysis. The OR represented the odds that wound healing will occur within six months, given a particular factor, compared to the odds of wound healing within six months occurring in the absence of that factor. An OR < 1 indicated a lower probability of wound healing within six months and an OR > 1 indicated a higher probability of wound healing within six months. Nagelkerke R Square was used to identify how well certain variables explain the variability in wound healing within six months or not.

The multivariate analysis was performed by calculating the area under the curve (AUC) of the receiver operating characteristics (ROC) curve. The ROC curve was generated by plotting the sensitivity (y-axis) against the 1-specificity (x-axis). The sensitivity indicated the number of patients with wound healing within six months who had been correctly classified. The 1-specificity indicated the number of patients classified as wound healing within six months but did not

have wound healing within six months. The AUC summarised the probability that the model was correct in distinguishing between patients whose wounds healed within six months and patients whose wounds did not.

The AUC guidelines ranged from 0 to 1, where an AUC of 1 indicated 100% correct predictions and an AUC of 0.5, 50% correct predictions. Table 4 shows the guidelines for discrimination [49].

Table 4 AUC guidelines for discrimination

AUC	*Guideline*
0.5	No discrimination
0.7	Poor discrimination
0.7–0.8	Acceptable discrimination
0.8–0.9	Excellent discrimination
> 0.9	Outstanding discrimination

Note: AUC= Area under the curve

2.4.3 Costs Associated with the Time to Wound Healing

To answer the third question, bar charts were created using Microsoft Excel. The bar charts represent the costs associated with the time to wound healing. Seven bar charts were created. One bar chart represented the total population and the other bar charts represented the following patients:

1) Patients with an amputation
2) Patients without an amputation
3) Patients with one surgery
4) Patients with redo surgeries
5) Patients with complications
6) Patients without complications

The bar charts for the costs included twelve variables, as shown below.

1) 'Admission Consults'
2) 'MRA'
3) 'CTA'
4) 'Duplex'
5) 'MRI'
6) 'CT'
7) 'X-ray'
8) 'Control consults'
9) 'Phone consults'
10) 'Gypsum consults'
11) 'Surgery'
12) 'Length of hospital stay'

The prices were multiplied by the number of times a resource was used, resulting in the cost per type of resource, which formed the bar chart. With the use of bar charts, the large dataset was summarised in a visual form, where trends were easier to highlight and accessible to a wide audience. The bar charts provided a clear overview of the resources, costs involved in the healing process, and the differences per patient. The distribution of the average costs for the total study population has been visualized on a pie chart. Eight other pie charts were created and represent the following patients:

1) Patients with an amputation
2) Patients without an amputation
3) Patients with one surgery
4) Patients with redo surgeries
5) Patients with complications
6) Patients without complications
7) Patients that experienced wound healing within six months
8) Patients that did not experience wound healing within six months

3. Results

This chapter discusses the socio-demographics, time to wound healing, factors that influence the time to wound healing within six months, and the costs related to the time to wound healing.

3.1 Socio-Demographics

1,784 patients were examined, and 1,081 excluded for the criterium of Rutherford classification 0,1, 2, and 3. After applying the other inclusion and exclusion criteria, 292 patients remained. Of these, 157 patients were excluded for having been treated conservatively, resulting in 135 patients included in the study (Figure 2). The socio-demographics of these patients can be found in Appendix E. The most important factors are mentioned below. The study population consisted of 91 men (67.4%) with an average age of 75 year (SD=9,9). Most of the patients were overweight (42.2%) or obese (25.2%) and 65.9% of the population had been diagnosed with DM. Most patients had arterial (49.6%) or diabetic ulcers (35.6%). Wounds located on the feet were the most common in this study (67.4%). Most patients had been referred to the WEC by general practitioners (74.1%). One third (33.3%) of the entire patient population had an amputation and 66.6% (N = 90) experienced wound healing. Twenty-seven-point four percent had a minor amputation and 11.9% a major amputation, and 7.4% of the patients had had two amputations. Postoperative complications included infection, (re-)occlusion, swelling, wound dehiscence, bleeding, or a no-healing tendency. Redo surgery was required by 27.4%, according the Clavien-Dindo classification 3.

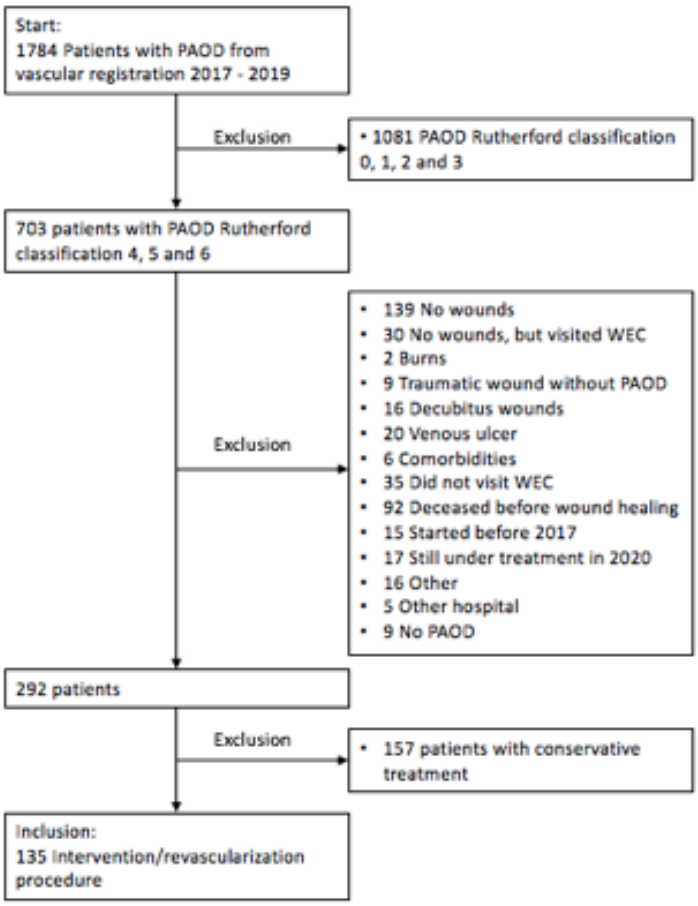

Figure 2 Flowchart in-exclusion criteria

3.2 Time to Wound Healing

The average time to wound healing for the total study population was 33 weeks (SD = 21.1). For patients who had had an amputation, the average time to wound healing for the amputation wound was 31 weeks (SD = 32.6) as opposed to 34 weeks (SD = 19.7) for patients who did not need an amputation. Of the total population, 71.1% had one surgery, and the average time to wound healing for these patients was 30 weeks (SD = 21.0), compared to 41 weeks (SD = 19.4) for patients who had to have redo surgeries. Patients with complications had a time to wound healing of 39 weeks (SD = 19.4), compared to 29 weeks (SD = 21.04) for patients without complications. The period of time between admission to the WEC and decision of treatment in the HOT was an average of seven weeks (SD = 9.6), while the time between the decision for treatment in the HOT and surgery was an average of four weeks (SD = 3.7). Figure 3 shows the timeline of the treatment process for PAOD patients treated in the WEC and HOT. Out of the study population, 96 (71.1%) patients required one surgery, 30 (22.2%) patients required two, six (4.4%) patients required three, and three (2.2%) patients required four surgeries. Figure 4 shows the bar chart for the total study population. The other bar charts can be found in Appendix F. In total, 90 (66.6%) patients experienced wound healing, of whom 40 (44.4%) patients experienced wound healing within six months.

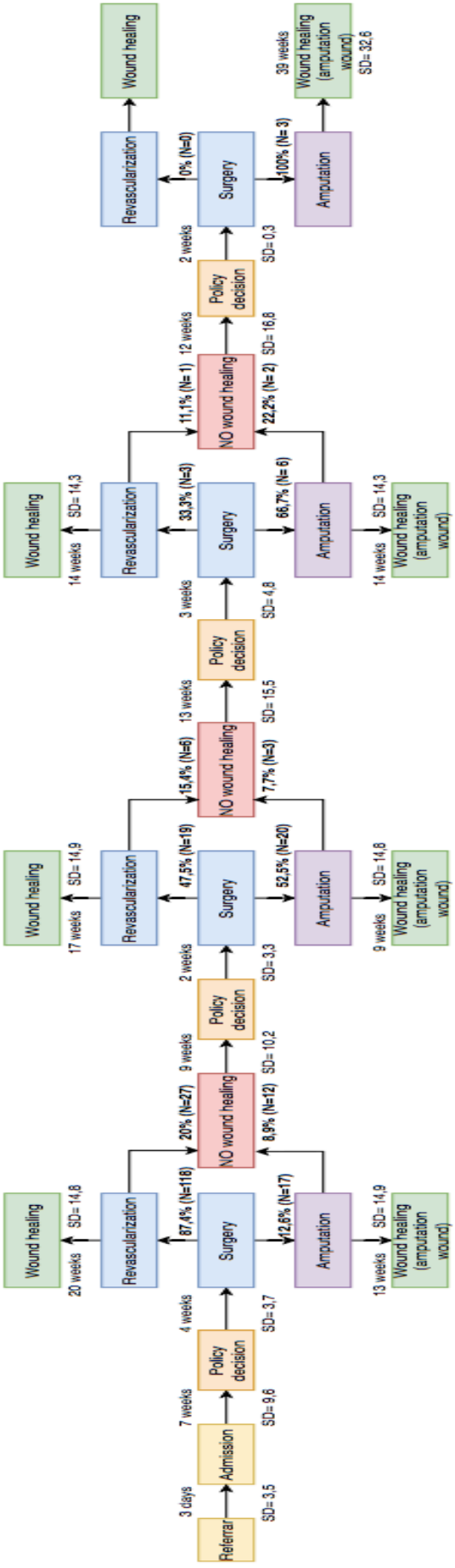

Figure 3 Timeline of treatment process for PAOD patients treated in the WEC and HOT

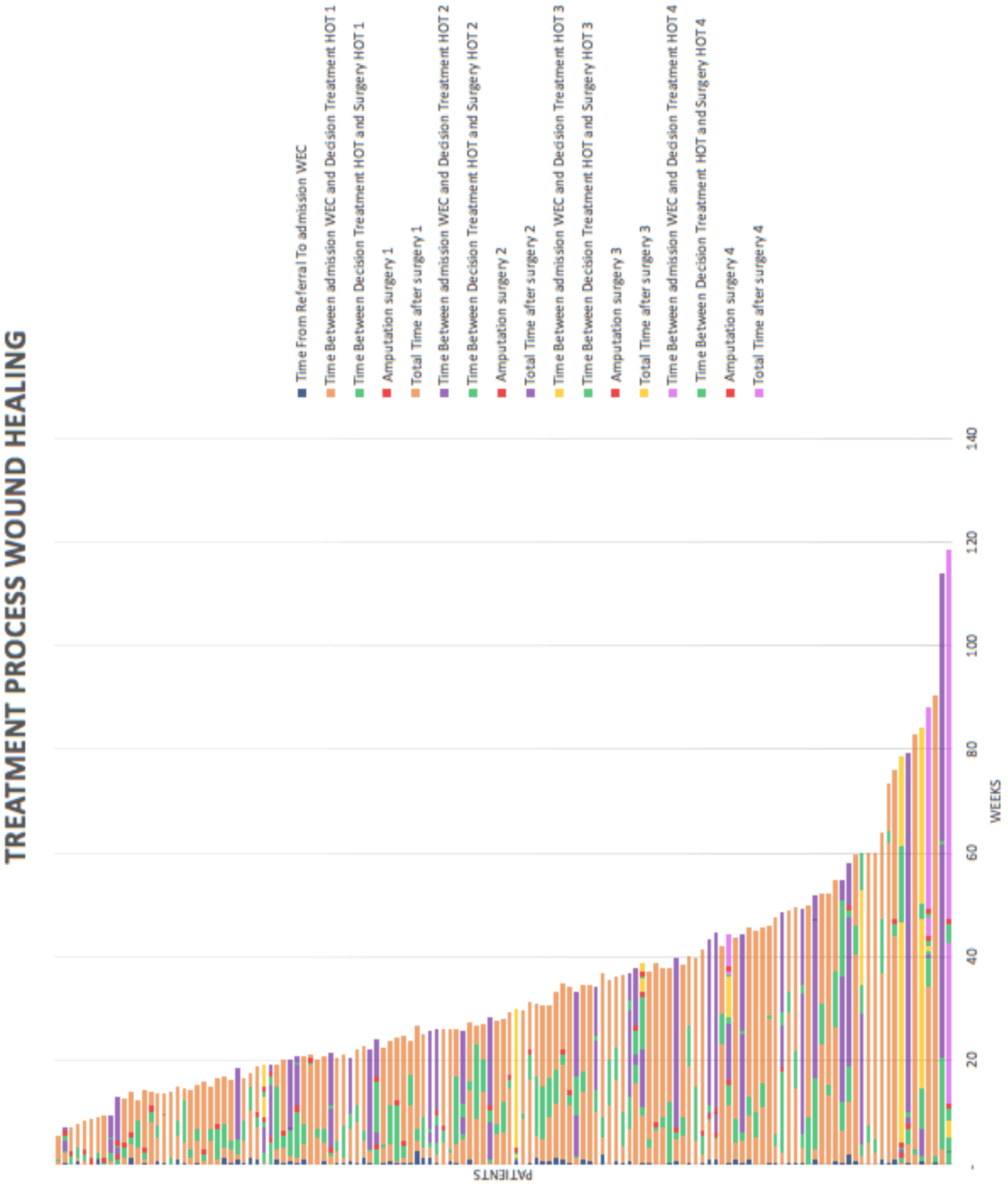

Figure 4 Bar chart of time from first admission consult to wound healing

3.3 Factors Related to Impaired or Improved Time to Wound Healing within six months

Variables used for the multivariate analysis were based on substantiations from three aspects: 1) expert opinion, 2) univariate analyses, and 3) the literature. This section discusses which variables have come out as important for each aspect. From the first sub-question, 40 patients experienced wound healing within six months, which resulted in including a maximum of four variables in the multivariate model to prevent overfitting.

3.3.1 Expert Opinion

Fifty percent (N = 2) of the vascular surgeons, 75% (N = 3) of the wound specialists and 63.6% (N = 7) of the surgical residents completed the survey. Table 5 presents the variables that were mentioned by the experts as relevant for time to wound healing and shows both the level of evidence and the number of experts who considered the specific variable to be relevant.

Table 5 Variables chosen as important by experts (ABI start = Ankle Brachial index, BMI= Body Mass Index)

Variables	Number (%)	Levels of evidence
Diabetes Mellitus	10 (83.3%)	multiple randomised clinical trials or meta analyses
Smoking	7 (58.3%)	multiple randomised clinical trials or meta analyses
Rutherford classification	7 (58.3%)	multiple randomised clinical trials or meta analyses
ABI start	7 (58.3%)	multiple randomised clinical trials or meta analyses
Revascularisation benefit	7 (58.3%)	Consensus of opinion of experts
Amputation risk	4 (33.3%)	Unknown
Age	4 (33.3%)	multiple randomised clinical trials or meta analyses
Wound location	3 (25%)	Unknown
Time from referral to admission WEC	3 (25%)	single randomised clinical trials or large non-randomised trails
Wound type	2 (16.7%)	single randomised clinical trials or large non-randomised trails
BMI	2 (16.7%)	Consensus of opinion of experts
Executing policy	2 (16.7%)	Consensus of opinion of experts
Comorbidity	2 (16.7%)	Unknown
Wound existence	2 (16.7%)	Unknown
Earlier return	1 (8.3%)	single randomised clinical trials or large non-randomised trails
Cardiovascular risk	1 (8.3%)	Consensus of opinion of experts

Note: ABI= Ankle Brachial Index, WEC= Wound Expertise Centre, BMI= Body Mass Index

3.3.2 Univariate Analyses

The significance levels, OR, confidence intervals, and the Nagelkerke R squares of the univariate analyses can be found in Table 6. The ANOVA test was used for the variables ‘specialists at admission’, ‘revascularisation benefit’, ‘open surgery’ and ‘additional surgery’. For the variables ‘cerebrovascular risk’, ‘referral by’, ‘additional examination’, ‘wound location’, ‘amputation risk’, ‘type of anaesthesia’, and ‘Clavien-Dindo classification’, the Welch test was used (Appendix G).

Table 6 Univariate analyses

Factor	OR (lower 95% - Upper 95%)	Sig	Nagelkerke R
Gender	0.994 (0.452–2.187)	0.998	0.000
Age	0.995 (0,959–1.003)	0.798	0.001
BMI	0.987 (0.918–1.061)	0.727	0.001
Smoking	1.487 (0.685–3.230)	0.316	0.011
Cardiac risk	0.464 (0.217–0.990)	0.047*	0.042
Hyperlipidaemia	0.970 (0.435–2.165)	0.941	0.000
Cerebrovascular risk: no			0.045
Cerebrovascular risk: TIA	0.195 (0.024–1.566)	0.124**	
Cerebrovascular risk: CVA	1.465 (0.445–4.822)	0.530	
Diabetes	0.692 (0.322–1.490)	0.347	0.009
Referral by: Within MST			0.041
Referral by general practitioner	2.189 (0.683–7.020)	0.187**	
Referral by other	0.708 (0.111–4.511)	0.715	
Wound existence (0-3 weeks vs. 4+ weeks)	1.147 (0.547–2.409)	0.716	0.001
Time from referral to admission WEC (0-2 days vs. 3+ days)	2.276 (0.994–5.210)	0.052**	0.050
Specialist on admission Vascular surgeon (V)+ nurse specialist(N)			0.004
Specialist on admission V + N + podo or revalidation	0.711 (0.214–2.366)	0.578	
Specialist on admission other	1.078 (0.398–2.923)	0.882	
Additional examination CTA + extra			0.039
Additional examination MRA + extra	1.394 (0.552–3.523)	0.483	
Additional examination other	0.590 (0.213–1.630)	0.309	
Earlier return	0.615 (0.279–1.356)	0.229	0.016
Admission consult (1 vs. more than 1)	0.279 (0.034–2.307)	0.236	0.020
Control consults before surgery (0-2 consults vs. more than 2 consults)	0.456 (0.215–0.996)	0.040*	0.044
Control consults after surgery 1 (0-5 consults vs. more than 5 consults)	0.220 (0.095–0.514)	0.000*	0.140
Phone consults	0,456 (0,186–1,117)	0.086**	0.030
Gypsum consults	0.120 (0.027–0.530)	0.005*	0.128
Total time until surgery	0.934 (0.885–0.987)	0.015*	0.082
Time between admission to WEC and decision for treatment HOT	0.910 (0.842–0.983)	0.016*	0.095
Time between decision treatment HOT and surgery HOT	0.970 (0.873–1.078)	0.575	0.003
MDO's (0-1 MDO vs. more than 1 MDO)	0.347 (0.132–0.913)	0.032*	0.054
Number of wounds (1 vs. 2)	0.571 (0.250–1.308)	0.185**	0.019
Type wound: Arterial ulcer vs. Diabetic/other ulcer + PAOD	0.350 (0.161–0.762)	0.008*	0.076
Wound direction (right vs. left)	1.125 (0.534–2.368)	0.756	0.001
Wound location: Dig 2-5			0.028
Wound location: Dig 1	1.485 (0.578–3.756)	0.404	
Wound location: Interdigit, forefoot, plantar, Lateral edge	0.979 (0264–3.627)	0.975	
Wound location: Lower leg, Ankle, Heel, Calf	2.187 (0.786–6.090)	0.134**	
Amputation risk: stage 4			0.028
Amputation risk: stage 1	2.143 (0.407–11.292)	0.369	
Amputation risk: stage 2	3.214 (0.634–16.291)	0.159**	
Amputation risk: stage 3	2.889 (0.562–14.843)	0.204	
Revascularisation benefit: stage 4			0.014
Revascularisation benefit: stage 1	0.758 (0.310–1.854)	0.543	
Revascularisation benefit: stage 2	0.521 (0.096–2.838)	0.451	
Revascularisation benefit: stage 3	1.157 (0.411–3.258)	0.782	
Location surgery (no or one level vs. multilevel)	1.221 (0.938–1.588)	0.138**	0.026
Open surgery: no			0.008
Open surgery: bypass	1.283 (0.352–4.675)	0.706	
Open surgery: fem-fem cross over	2.565 (0.154–42.752)	0.512	
Open surgery: removal of obstruction	1.222 (0.500–2.986)	0.661	
Open surgery: More than one open surgery	0.855 (0.161–4.548)	0.854	
Additional surgery: No			0.391
Additional surgery: Wound toilet	0.438 (0.157–1.221)	0.114**	
Additional surgery: Amputation (s)	0.000 (0.000)	0.997	
Additional surgery: Other	0.072 (0.009–0.585)	0.014*	
First operator at surgery: Vascular surgeon vs Surgical resident	2.667 (0.869–8.185)	0.086**	0.030
Second operator at surgery: Vascular surgeon vs. Surgical resident	0.625 (0.158–2.470)	0.503	0.017
Number of assistants at surgery	0.785 (0.420–1.469)	0.449	0.006
Kind of anaesthesia: ITN			0.013
Kind of anaesthesia: Balanced	0.885 (0.337–2.170)	0.742	
Kind of anaesthesia: Other	0.493 (0.130–1.867)	0.298	
Complication	0.276 (0.121–0.627)	0.002*	0.106
Operation time	1.312 (0.612–2.813)	0.484	0.005
Number of surgeries	0.422 (0.192–0.926)	0.031*	0.063
Clavien-Dindo classification: None			0.112
Clavien-Dindo classification: No need for pharmacological treatment.	0.143 (0.017–1.180)	0,071**	
Clavien-Dindo classification: Requiring pharmacological treatment (antibiotics)	0.239 (0.050–1.146)	0.073**	
Clavien-Dindo classification: Requiring surgical endoscopic or radiological intervention	0.334 (0.130–0.861)	0.023*	
Length of Hospital stay	0.915 (0.857–0.997)	0.008*	0.114
Start ABI right	1.001 (0.993–1.010)	0.725	0.001
Start ABI left	0.996 (0.986–1.005)	0.389	0.009
Rutherford classification right	0.640 (0.275–1.487)	0.299	0.018
Rutherford classification left	0.987 (0.407–2.392)	0.978	0.000

Note: *p < 0,05 **p < 0,2, OR = odds ratio, BMI = body mass index, TIA = transient ischemic attack, CVA = cerebrovascular accident, MDO = multidisciplinary meeting, ITN = intrathecal narcotics, ABI = ankle brachial index

3.3.3 Multivariate Analysis

The factors used for the multivariate analysis were examined with two criteria; the univariate analysis (ANOVA) test had to show a significant level below 0.2, and the variable had had to be reported by previous studies or in the expert opinion. Table 7 shows the variables that met the criteria of $p < 0.2$ in the univariate analyses. Wherever an 'X' is depicted, it means that the variables used were mentioned in the literature or in the expert opinions.

Table 7 Substantiation of chosen variables for multivariate analysis

Univariate analyses	Expert opinion	Literature
Cardiac risk		X
Cerebrovascular risk		
Referral by		
Time from referral to admission WEC		
Additional examination		
*Wound type	X	X
Number of wounds		
Control consults before surgery 1		
Control consults after surgery 1		
Phone consults		
Gypsum consults		
MDOs		
Total Time Until Surgery		
*Time Between admission WEC AND decision treatment HOT	X	
Number of surgeries		
Additional surgery		
Location surgery		
First operator at surgery: vascular surgeon vs. surgical resident		
*Complications		X
Clavien-Dindo classification		
Length of hospital stay		

Note: *= variables chosen for multivariate analysis, MDO= Multidisciplinary Meeting, WEC= Wound Expertise Centre, HOT= Hybrid Operating Theatre

The variables used in the multivariate analysis were 'wound type', 'time between admission to WEC and decision for treatment HOT', and 'complications' (Table 8). The variable 'wound type' was used because previous studies showed a difference in time to wound healing between patients with an arterial ulcer as compared to patients with a diabetic foot ulcer [35-41]. In addition to the literature, 83.3% of the experts thought that there was an association between the time to wound healing and diabetic foot ulcers. Previous studies did not show whether the variable 'time between admission to the WEC and decision treatment HOT' was associated with time to wound healing. However, the univariate analysis showed a significantly lower probability of wound healing within six months for patients with a longer time between admission to the WEC and the decision for treatment in the HOT. In addition, six (50%) experts' opinions associated this factor with a longer time to wound healing. The variable 'complications' was used in the model because the univariate analysis of complications showed a significance level below 0.05. Previous studies showed that complications are caused by several diseases and health conditions, such as type 2 Diabetes, coronary heart disease, and obesity, which can cause a delay in wound healing [35-41]. The experts did not mention the variable 'complications' as relevant. However, the experts did mention the factors that can cause complications, such as 'smoking', 'DM' and 'BMI'. 'Cardiac risk' was excluded from the multivariate analysis because 'cardiac risk' showed no significant effect in the multivariate analysis.

Table 8 Multivariate Model

	Sig.	OR (lower 95% - Upper 95%)
Wound type	0.021*	0.366 (0.156–0.857)
Time between admission WEC and decision treatment HOT	0.026*	0.909 (0.836–0.989)
Complications	0.001*	0.219 (0.091–0.527)
Nagelkerke R Square	0.258	

Note: *p<0,05, WEC= Wound Expertise Centre, HOT= Hybrid Operating Theatre

The model accounts for 25.8% of the variability in wound healing within six months and showed an AUC of 0.766 (95% 0.681 – 0.851, SD = 0.043, Sig = 0.000).

3.4 Costs Associated with the Time to Wound Healing

The average cost per patient in this study population for the wound healing process was €12,222 (SD = 7,499). Figure 5 shows the pie chart of the total study population. Most of the costs were for surgeries (Avg., €6,226; SD = 4,886) and the length of hospital stay (Avg., €4,524; SD = 3,811), followed by the cost for control consults (Avg., €649; SD = 425) and the additional examinations MRA (Avg., €104; SD = 111.80). MDOs represented the least costs (Avg., €71.66; SD = 58.10). Appendix H.1 shows the pie charts created for wound healing within six months versus no wound healing within six months, one surgery versus redo surgeries, no amputation versus amputation, and no complications versus complications. The average cost for the treatment process was €12,210 (SD = 7,526) for patients whose wounds healed within six months and €12,285 (SD = 7,490) for patients whose wounds did not heal within six months.

Figure 6 shows the bar chart for the costs associated with the time to wound healing for the total study population. Appendix H.2 shows the bar charts for costs associated with the time to wound healing for the patients who had an amputation or not, complication or not, and redo surgeries or not. The average cost for patients who had an amputation, a complication, or a redo surgery were, respectively, €14,584 (SD = 9,690), €16,001 (SD = 8,534), €19,003 (SD = 7,382). The costs for patients who did not have an amputation, a complication or a redo surgery were, respectively, €11,041 (SD = 7,481), €9,703 (SD = 7,499), €9,467 (SD = 4,569).

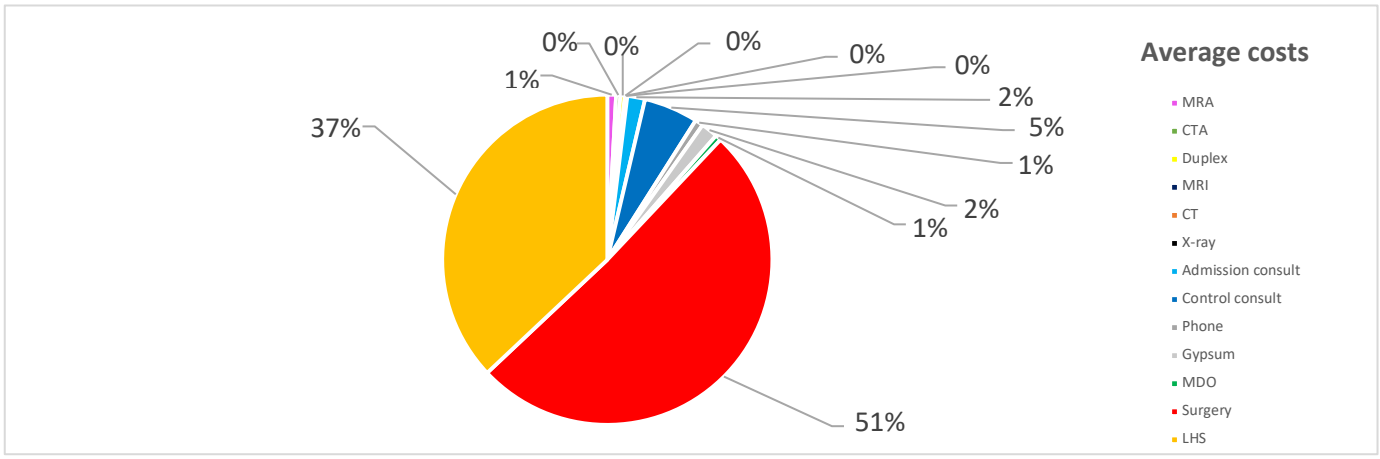

Figure 5 Cost distribution wound healing process (LHS= Length of hospital stay , MDO= Multidisciplinary meeting)

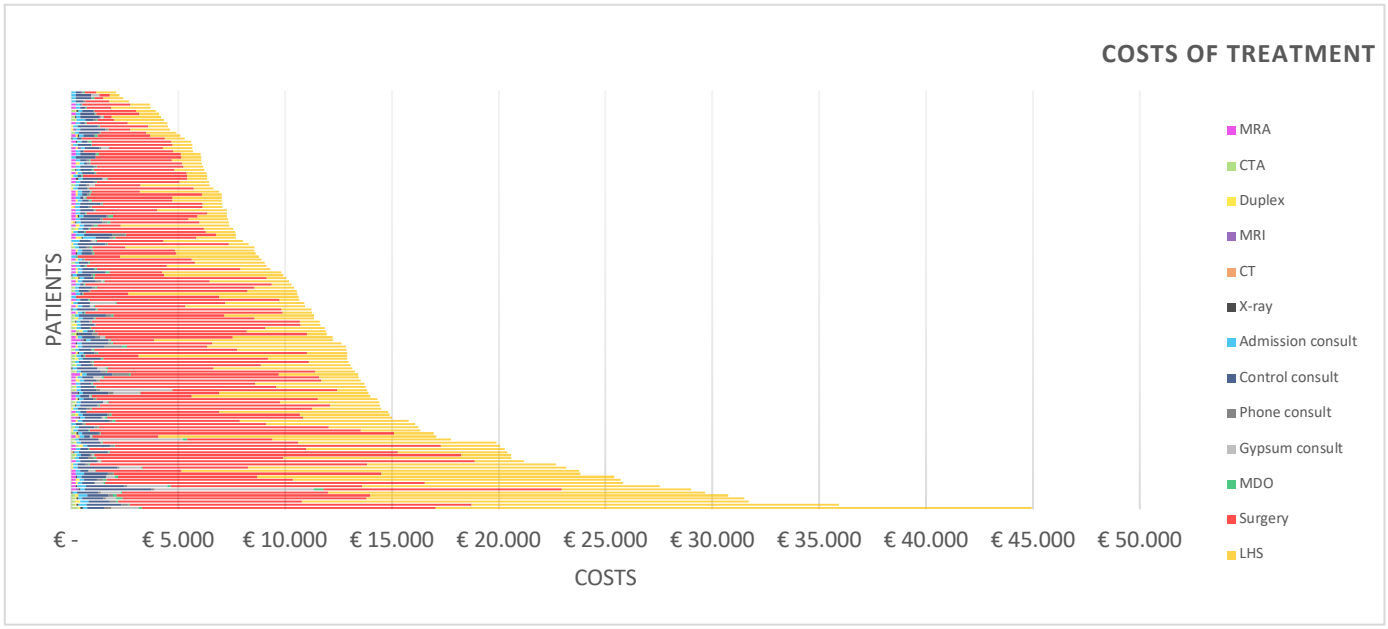

Figure 6 Bar chart of costs associated with time to wound healing (LHS= Length of hospital stay , MDO= Multidisciplinary meeting)

4. Discussion

4.1 Time to Wound Healing

In this study of patients with PAOD and tissue loss, complete wound healing was observed in 90 patients (66.6%), of whom 40 (44,4%) healed within six months. Currently, there are no previous studies regarding patients with PAOD who were treated in the WEC and underwent interventions in the HOT. Previous studies mainly focused on wound healing following a specific intervention, either involving bypass surgery or EVT. Five previous studies did observe wound healing within six months for patients who had had revascularisation, with healing ratios between 5% and 85.5% [36–38;40;42]. The variation of healing ratios between the previous studies and this study can be explained by the different patient characteristics, wound characteristics, and type of interventions (Table 9).

Table 9 Current and previous studies with corresponding study population, healing ratio within six months, % male, average age, % DM, average BMI, % smoking, wound location and surgery type.

	Current study	**Azuma et al**			**Chung et al**	**Kobayashi et al**			**Soderstorm et al**	**Krishna et al**
Study population	N = 135	N = 249			N = 334	N = 177			N = 150	N = 97
Healing ratio 6 months	44.4%	Overall 72.2%			42%	64%	36%	5%	40%	56.3%
		Non-ESRD* 85.5%	ESRDnorALB* 68%	ESRDlowALB* 40%						
Age (Mean +- SD)	75 +- 9.9	67 (36–91)			68	73 +- 10	73 +- 8	71 +-13	76 (44-95)	75.5 +- 9.3
Diabetes	65.9%	81%			66%	71%	82%	78%	50%	66.7%
BMI **% BMI > 25**	26.8 +- 5.2 67.4%	X			X	22 +- 4	20 +- 3	20 +- 3	44%	X
Smoking (%)	63%	X			51%	42%	29%	43%	X	53.3%
Wound location	67.4% Toe 12.6% Interdigit, forefoot, plantar 20% Heel/ leg	X			62.2% Forefoot 29.6% Single digit 13.3% Multiple digit 8.9% Midfoot 16.3% Heel 6.7% Malleolus 5.9%. Global	Toe	Heel	Extensive wounds on the fore or mid-foot along the dorsal or plantar surface	Leg ulcers	45.5% toe
Surgery type	Bypass/ EVT	Distal bypass			Infrainguinal bypass	EVT			Infrainguinal bypass	PTA + stent

Note: All patients in the studies had PAOD with tissue loss. non- ESRD: patients without ESRD; ESRDnorALB: ESRD patients without severe low albuminemia; ESRDlowALB: ESRD patients with severe low albuminemia [36-42]

Azuma et al. observed that patients with end-stage renal disease (ESRD) have lower healing rates (68%;40%) as compared to patients without ESRD (85.5%). In addition, patients with severely low albuminemia (ESRDlowALB) and ESRD have a lower healing ratio (40%) as compared to patients without severely low albuminemia (ESRDnorALB) (68%). This study did not analyse ESRD and the level of albuminemia. Furthermore, it was observed that more patients in Azuma et al.'s study had been diagnosed with DM (81%) as compared to the population of this study (65,9%). Based on these factors, a lower wound healing rate was expected in Azuma et al.'s study as compared to this study. However, this study defined time to wound healing as the time from admission to the WEC. According to Azuma et al., the time to wound healing started after the intervention [37]. Moreover, the average age of the population in that study was lower (67) as compared to this study (75). These reasons could explain the higher healing ratio (72,2%) as compared to this study (44,4%).

The percentage of smokers (51% versus 63%) and the average age (68 versus 75) are lower in Chung et al.'s study as compared to this study. These characteristics are conducive to a shorter time to wound healing. Therefore, a higher healing ratio was expected in Chung et al.'s study, as compared to this study. Furthermore, every patient in Chung et al.'s study had undergone bypass surgery, while in this study, multiple revascularisation techniques were analysed. This study observed that only 8,9% of the first surgeries were bypasses. This percentage increased for patients with redo surgeries. Previous studies have shown that patients who had had bypass surgery had a longer recovery period as compared to patients who had had less invasive EVTs [52–53]. The bypass surgeries could explain why the healing ratio in Chung et al.'s study (42%) is close to the ratio in this study (44.4%) [34].

Kobayashi et al. made a distinction between wounds located on the toe, heel, or forefoot [38]. Kobayashi et al. observed that wounds located on the toe have the fastest recovery rate (64%) and wounds on the forefoot the slowest (5%). The majority of the wounds in this study were located on toes (67.4%), and, according to Kobayashi et al., these have a faster recovery time. Therefore, the same healing ratio was expected as in the section of Kobayashi et al.'s study that focused on wounds on the toe. However, the average BMI (22) and percentage of smokers (42%) were lower in Kobayashi et al.'s study, as compared to this study (26.8; 63%). This could explain the higher healing ratio in Kobayashi et al.'s study (64%), as compared to this study (44,4%).

Soderstorm et al. only analysed wounds located on the legs [40]. In comparison, this study only observed 20% leg ulcers. Leg ulcers usually have larger wound surfaces which require a longer time to heal [54]. Therefore, it was expected that the healing ratio would be much lower in Soderstorm et al.'s study as compared to this study. However, the percentages of patients with a diagnosis of DM (50%) or a high BMI (44%) were lower in Soderstorm et al.'s study [40] as compared to this study (65.9%; 67.4%). This could explain why the healing ratio in Soderstorm et al.'s study (40%) is close to the ratio in this study (44.4%).

The type of intervention utilised in Krishna et al.'s study was EVT [42]. In addition, Krishna et al.'s study had fewer smokers (53.3%) in the study population as compared to this study (63%). These factors could explain the higher healing ratio in Krishna et al.'s study (56.3%) as compared to this study (44.4%).

In conclusion, the remarkable differences in wound healing ratios at six months in the previously mentioned studies were due to differences in patient characteristics, wound location, and wound duration prior to intervention. This means that the performance of the WEC cannot be judged through a direct comparison of the results of the previous studies with the results of this study. Not all information regarding the patients and the wound characteristics is available in certain studies, which further hampered a comparison of the results. Further research should focus on reporting standards based on patient and wound characteristics (e.g., size, location, depth).

The patients who enter the WEC already have impaired wound healing because the wound did not heal within two weeks. In addition, the patients had to undergo an intervention. The combination of these factors made it difficult to accomplish wound healing within six months. This study revealed a healing ratio among the range of the previous studies. For this reason, it can be assumed that the WEC is doing well but still has potential to improve. This study revealed several factors that influence wound healing within six months in the WEC. If these factors are addressed, it is feasible that the healing ratio will increase. This is further explained in the following paragraph.

4.2 Factors Related to Impaired or Improved Time to Wound Healing within six months

The factors significant in the univariate analyses will not be further discussed, due to the limitations of the univariate analyses. The limitations were that the probability of obtaining a significant result due simply to chance was high, and the factors were not corrected for confounders.

The factors 'wound type', 'time between admission WEC and decision treatment HOT' and 'complications' were significant in both the multivariate analysis and the univariate analysis. This study observed that diabetic foot ulcers, a long time between admission to the WEC and decision for treatment in the HOT, and a complication decreased the probability of experiencing wound healing within six months.

This study observed a 63.4% smaller probability of wound healing within six months in patients with a diabetic foot, as compared to patients without. This observation is supported by previous findings [36-42]. In addition, patients with a diabetic foot also have a 10 times higher chance of having an amputation [14]. People with DM often do not notice or are not bother by wounds on their feet due to neuropathy, which is a type of nerve damage caused by high blood sugar levels [56]. This could lead to severe complex wounds, with delayed admission to the WEC. Currently, patients who have severe complex wounds and diabetic foot are receiving additional care, provided by dieticians and podiatrists, in the WEC. The WEC can change this policy by providing additional care to not only patients with severe complex wounds, but to all patients with a diabetic foot admitted to the WEC. This will ensure optimal conditions for the wound healing process and reduce the time to wound healing.

For patients with a longer time between admission to the WEC and the decision for treatment in the HOT, there was a 10% lower probability of wound healing within six months, according to the findings in study. This is also supported by Chung et al., who observed a delay in wound healing with a delay in intervention [37]. During the time between admission to the WEC and the decision for treatment in the HOT, other wound treatments, which may not improve wound healing, may be utilised, which may delay the time to wound healing. Previous studies showed that the longer it takes for a wound to improve, the greater the chances of an increase in the complexity of the wound, which results in a longer time to wound healing. In addition, the increased complexity of the wound may result in an amputation instead of a revascularisation [57-58]. Moreover, our study showed that the average duration for the time between admission to the WEC and the decision for treatment in the HOT was seven weeks for several reasons, for example the higher average age of the patients in this study (75). Older patients may choose not to undergo surgery as the benefits of wound healing may not outweigh the risk of complications from surgery. The WEC aims to provide the most effective wound treatment, utilising surgery only when necessary.

Another reason could be that an MDO is not planned for every patient by default, only for those with severe complex wounds and when the specialist is undecided regarding the treatment. Currently, for the most part, a surgeon and a wound care specialist are present during an admission to the WEC, and an MDO is only requested for severe complex wounds once a week. Consequently, a treatment assigned to a patient may not always be reviewed by different specialists. For these reasons, the most effective care may not be immediately administrated to each patient, which can lead to the decision for treatment in the HOT and the treatment itself to be postponed, therefore, increasing the time to wound healing. If the wound does not improve, the WEC should always request an MDO during the treatment process. It is important that the expertise of these various specialists is combined at all times and not only for severe complex wound cases. This could ensure that patients receive the most effective treatment immediately, resulting in a reduced time to wound healing. The viability of scheduling more MDOs and involving more surgeons during the wound healing process requires additional research.

This study found that patients who have had a complication have a 78.1% smaller chance of achieving wound healing within six months. Forty percent (N = 62) of the study population experienced complications. Most of the complications were infections (32.3%, N = 20). Prompers et al. and Lawrence et al. observed that wound infection is an important predictor for non-healing wounds, and that it is associated with higher amputation rates, redo surgeries, and increased hospitalisation [34-35]. Previous studies observed that readmissions are associated with a longer time to wound healing and are mostly due to complications [59-62]. Factors that influence readmission after revascularisation are female gender, hypertension, cardiac risk, DM, renal insufficiency, smoking, obesity, and bypass surgery [59-62]. No literature was found regarding which factors influence complications after revascularisation for patients with PAOD specifically. Further research is required to determine which factors are associated with complications. If factors associated with

complications were known, the WEC would be able to manage these risk factors more efficiently to prevent complications, resulting in a reduced time for wound healing.

The multivariate model of the three factors showed an AUC of 0.77. The model had an acceptable discrimination and almost excellent discrimination (0.7–0.8), with a 78% chance that the model would be able to distinguish between patients whose wounds heal within six months and patients whose wounds do not heal within six months. However, there is still room for improvement in the model, which can be done by increasing the study population and including more predictors. In addition, more research can be done to analyse other factors associated with the time to wound healing, such as renal insufficiency and hypertension, as observed in previous studies. Renal insufficiency and hypertension were not included in this study but can be found in the vascular database and patient files.

4.3 Costs Associated with Time to Wound Healing

The costs for patients whose wounds healed within six months (€12,210; SD = 7,490) and patients whose wounds did not heal within six months (€12,285; SD = 7,526) were similar. There was no relative difference in costs for admission consults, control consults, additional examination (e.g. MRA, CTA, Duplex, MRI, CT, X-ray), surgeries, and hospitalisation. The similarity in the total average costs for these groups could be explained by the fact that patients may receive personalised wound care at different stages during the wound healing process. Some patients may have invasive treatments, associated with high costs, at the start of the wound healing process, and other patients may have the same type of invasive treatment later on during the wound healing process. However, patients could also have several less invasive treatments that cost the same as the invasive treatment. The cost of surgery differs per type of surgery, with costs ranging between €5,146 for bypass surgery and €1,881 for a PTA.

The total average treatment cost increased for patients who had an amputation (€14,584; SD = 9,690), patients who had a complication (€16,001; SD = 8,534), or patients who had redo surgery (€19,003; SD = 7,382), as compared to patients who did not have an amputation (€11,041; SD = 7,481), patients who had no complication (€9.703; SD = 7,499), or patients who had no redo surgery (€9,467; SD = 4,569). The distribution of the total cost for these patients differed in regard to the costs for hospitalisation and surgeries. The groups of patients who had an amputation, a complication, or redo surgery had relatively more costs for hospitalisation (37%, 41%, 49% versus 29%, 37%, 37%) and relatively less costs for surgery (51%, 47%, 40% versus 58%, 51%, 51%) as compared to patients who did not have an amputation, a complication, or redo surgery. This could be explained by the fact that the patient group who had amputation, a complication, or redo surgery need longer recovery periods and hospitalisation as compared to patients who did not have those problems. This is also supported in previous studies [62-63]. Preventing amputations, complications, and reducing the number of redo surgeries could reduce the time to wound healing and decrease the total costs by approximately €4,960, €6,298 and €9,356. The savings are a rough indication; this comparison is based on the average differences in costs between patients who did and did not have amputation, complications, or redo surgery.

The higher standard deviation of the total average cost for patients with amputation, complications, or redo surgery could be explained by the fact that patients receive personalised wound care that involves different costs. Patients can develop different complications, which require different treatments. There are also different types of amputation, with costs ranging between €2,069 for an above-knee amputation and €938 for an amputation in the tarsus of a toe.

4.4 Limitations

The first limitation of this study was in the data collection method. The data was collected retrospectively with the associated known limitations, such as missing and incorrect data. The limitations of a retrospective study were contained to an extent by the two researchers who accurately examined the data used for the study. The researchers first examined the data of a number of patients together. Once the examination was completed, an agreement was entered into on how much and which data should be included in the study. In the event of uncertainties, the two researchers consulted with each other.

The second limitation was the relatively small study population, which made it difficult to divide the patients into subgroups. During this study, it was not possible to discover whether there is a difference in wound healing among different wound locations. Previous studies did show that some wounds, especially on the heel or fore foot, require a longer time to heal as compared to other wound locations [36-42]. A larger study population allows for the creation of more subgroups. This means that it would no longer be necessary to combine groups, which creates more certainty in the outcomes.

The third limitation was that the factors hypertension and renal insufficiency were not taken into account in this study. Previous studies observed that hypertension and renal insufficiency were important factors for the time to wound healing in general. Some of the previous studies did not take into account other factors, such as cardiovascular diseases, which is also an important factor in determining whether or not it is possible to achieve wound healing within six months. Further research should also include the factors hypertension and renal insufficiency.

The last limitation was regarding the external validity of the model, which was not assessed in this study. As a result, it was not yet possible to determine whether the model of this study would perform the same in a different population. Further research should test the model on another population with similar characteristics to establish whether the results are externally valid.

4.5 Recommendations

The recommendations resulting from this study are divided into recommendations for the WEC and recommendations for further research. The recommendations for the WEC are related to admission to the WEC and decisions regarding surgery in the HOT. The recommendations for further research are related to reducing complications and the viability of scheduling more MDOs and consult a surgeon more frequently during the wound healing process. The aspects are shown in Figure 7.

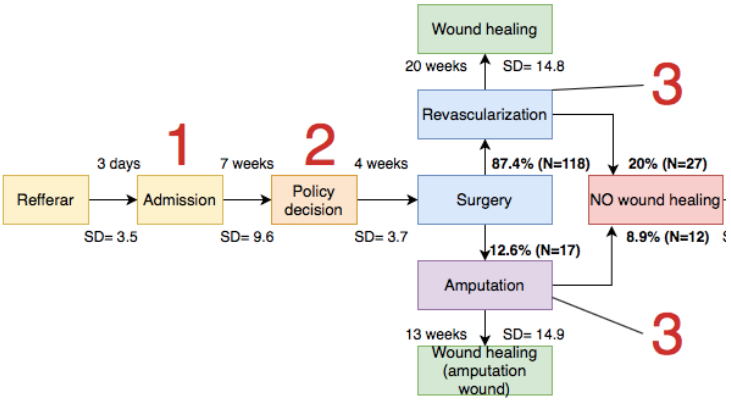

Figure 7 Overview recommendations follow process (1: admission WEC; 2: decisions for surgery HOT; 3: occurrence of complications)

4.5.1 Recommendations WEC

The recommendations for the WEC are aimed at managing the care for patients with a diabetic foot more carefully at the start of the wound healing process and decreasing the time between admission and surgery in the HOT, resulting in a reduced time to wound healing (Table 10).

Table 10 Recommendations WEC

From admission	**Recommendation**
Patients with diabetic foot at admission	Patient need to be referred to the dietician and podiatrist immediately after admission
During decision process	**Recommendation**
No wound improvement after two weeks	Request MDO
No wound improvement after four weeks	Surgeon must be present at the next control consult
No wound improvement after six weeks	Requesting MDO and surgeon must be present at the next control consult

A shorter time between admission to the WEC and a decision regarding an intervention will increase the probability of wound healing within six months due to timelier treatment. However, this will not automatically lead to a reduction in the average cost per patient, which was based on the differences between the average costs for patients whose wounds healed within six months and patients whose wounds did not. The opportunity for planning MDOs by default and providing additional care for all the patients with a diabetic foot entering the WEC will not lead to a significant increase in additional costs. This is due to the low cost of MDOs (€50.92) and control consults (€52.00) compared to the total cost for the entire treatment process (€12,248). Further research is required to establish whether it is viable to schedule more MDOs and consult a surgeon more frequently during the wound healing process.

4.5.2 Recommendations Further Research

The recommendations for further research are aimed at reducing complications and the viability of scheduling more MDOs and consult a surgeon more frequently. Two studies can be conducted to establish whether the WEC is able to reduce complications and schedule more MDOs and consult a surgeon more frequently, resulting in a reduced time to wound healing (Table 11).

Table 11 Recommendations further research

Study	Explanation
Investigating factors associated with the occurrence of complications	With the use of a logistic multivariate analysis, factors that are associated with the occurrence of complications can be predicted. If the WEC knows which factors play a role in the occurrence of complications, it can intervene from the start of the treatment to prevent complications.

Study	Explanation
Modelling the MDOs and surgeons during the care pathway during the time to wound healing in the WEC and HOT	With the use of a simulation model, it would be possible to gain insight into whether it is viable to schedule more MDOs and surgeon consults during the time to wound healing in the WEC.

The prevention of complications may result in an increased possibility of wound healing within six months and a decrease in average cost per patient of approximately €6,298.

6. Conclusion

This study answered the question: *Which factors influenced the time to wound healing and the cost for patients with PAOD who received wound care in the WEC and underwent an intervention in the HOT of MST?*

Factors that have a negative influence on wound healing within six months are a diabetic foot, time between admission to the WEC and the decision for treatment in the HOT, and the occurrence of complications. To reduce the time to wound healing, the WEC should focus on optimal management of the care given to diabetic foot patients and diminishing the time from admission to the WEC to revascularisation in the HOT. Further research should focus on the possibility of reducing the number of complications in the WEC. In addition to major amputations, the occurrence of complications and the number of surgeries are associated with higher costs.

The findings and recommendations of this study can make a difference in patient's live and the costs of caring for patients with complex wounds and PAOD in the WEC and HOT.

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8. Appendix

Appendix A Variables collected

Variable	Variable
PatientID	Number of multidisciplinary meeting
Age	Rutherford classification right
Gender	Rutherford classification left
Risk profile smoking	E/A index right start
Risk profile Cardiac	E/A index right end
Risk profile hyperlipidaemia	E/A index left start
Risk profile Cerebrovascular	E/A index left end
Risk profile Diabetes	Number of wounds
Diabetic type	Type wound1,2
Diabetic Since	Wound1 right/ left1,2
BMI	Location wound1,2
VAS start rest	Amputation Risk1,2
VAS start movement	Revascularization benefit1,2
VAS end rest	Number of operations
VAS end movement	Normal operating theatre
Referral by	Hybrid operating theatre (HOT)
Date Referral	Date operation1,2,3,4
Wound existence	Operation type1,2,3,4
Date first consult WEC	Vascular surgeon1 1,2,3,4
Date last consult WEC	Vascular surgeon2 1,2,3,4
Improvement within 6 months	Anaesthesiologist 1,2,3,4
Vascular surgeon	Number of assistants1,2,3,4
Nurse specialist	Start time operation1,2,3,4
Podotherapist	End time operation1,2,3,4
Revalidation specialist	Kind of anaesthesiology1,2,3,4
Other	Complications during operation1,2,3,4
Additional Examination	Type complications1,2,3,4
MRA	Clavien-Dindo classification
CTA	Length of hospital stay
Duplex	DBC-code
MRI	Care product1
CT	Care product2
X-ray	Care product3
Other	Care product4
Earlier return	Care product5
Number of admission consults	Care product6
Number of control consults before surgery	Care product7
Number of control consults after surgery1	Care product8
Number of control consults after surgery2	Number of DBC-codes
Number of control consults after surgery3	
Number of phone consults	
Number of gypsum consults	

Appendix B Variables per category

Variables	***Categories***
Gender	1) Male 2) Female
Smoking	1) Yes 2) No
Cardiac Risk	1) Yes 2) No
Cerebrovascular risk	1) TIA 2) CVA 3) No
Hyperlipidaemia	1) Yes 2) No
Diabetes	1) Yes 2) No
Wounds	1) 1 wound 2) 2 wounds
Wound existence	1) 0-3 weeks 2) 4-8 weeks 3) More than 8 weeks
Wound direction	1) Right 2) Left
Type wound	1) Arterial ulcer 2) Diabetic ulcer 3) Burns, traumatic ulcers, pressure ulcers.
Location wound	1) Dig 1 2) Dig 2-5 3) Interdigit, forefoot, plantar and lateral edge 4) Lower leg, Ankle, Heel, Calf
Amputation risk	1) Stage 1 2) Stage 2 3) Stage 3 4) Stage 4
Revascularization benefit	1) Stage 1 2) Stage 2 3) Stage 3 4) Stage 4
Referral by	1) Within MST 2) General Practitioner 3) Podotherapists, home care organization, Mediant
Access time	1) 0-2 days 2) More than 2 days
Specialists during admission	1) Vascular surgeon (V)+ nurse specialist(N) 2) V + N + podo + Revalidation 3) Other
Additional examination	1) CTA + extra 2) MRA + extra 3) Other
MDO's	1) 0-1 MDO 2) More than 1 MDO
Earlier return	1) Yes 2) No
Admission consult	1) 1 admission consult 2) More than 1 admission consult
Control before surgery	1) 0-2 control consults 2) more than 2 control consults
Control consults after surgery	1) 0-5 control consults 2) more than 5 control consults
Phone consults	1) Yes 2) No
Gypsum consults	1) Yes 2) No
Location surgery	1) None or one level revascularization 2) Multilevel revascularization
Open surgery	1) Bypass 2) Fem-fem cross over 3) Desobstruction 4) More than one open surgery 5) No
Additional surgery	1) Wound toilet 2) Amputation (s) 3) Other
Vascular surgeon1	1) Vascular surgeon 2) Surgical resident
Vascular surgeon2	1) Vascular surgeon 2) Surgical resident
Kind of anaesthesia	1) ITN 2) Balanced 3) Other
Complication	1) Yes 2) No
Clavien-Dindo Classification	1) No need for pharmacological treatment (Normal course) 2) Requiring pharmacological treatment (antibiotics) 3) Requiring surgical endoscopic or radiological intervention 4) No

Appendix C Variables for Univariate analyses

Variable	Variable
PatientID	E/A index left start
Age	Number of wounds
Gender	Type wound1
Risk profile smoking	Wound direction1
Risk profile Cardiac	Location wound1
Risk profile hyperlipidaemia	Amputation Risk1
Risk profile Cerebrovascular	Revascularization benefit1
Risk profile Diabetes	Number of operations
Diabetic type	Time determining policy1
BMI	Time executing policy1
Referral by	Waiting time operation1
Access time	Surgery: Location1
Wound existence	Surgery: Open1
Heal time within six months	Surgery: Additional1
Specialist(s) @ admission	Vascular surgeon1
Additional Examination	Vascular surgeon2
Earlier return	Number of assistants1
Number of admission consults	Operation time
Number of control consults before surgery	Kind of anaesthesiology1
Number of control consults after surgery1	Type complications1
Number of phone consults	Clavien-Dindo classification1
Number of gypsum consults	Total Length of hospital stay
Number of multidisciplinary meeting	
Rutherford classification right	
Rutherford classification left	
E/A index right start	

Appendix D Survey Expert opinion

Treatment process in the Wound Expertise Centre (WEC) in combination with the Hybrid Operating Theatre (HOT) of patients with Peripheral Arterial Disease in the Medisch Spectrum Twente

Ik ben Isabelle en studeer Health Sciences aan de Universiteit Twente. Momenteel ben ik bezig met het onderzoeken hoe het behandeltraject in het wondexpertise centrum in combinatie met de hybride OK kan worden geoptimaliseerd. Hierbij richt ik mij op de patiëntengroep met Perifeer vaatlijden. Om het behandeltraject te optimaliseren heb ik het huidige behandeltraject in kaart gebracht waarna ik nu bezig ben met het analyseren van deze gegevens. Een uitkomst waar ik naar kijk binnen dit behandeltraject is de wondgenezingstijd. Met behulp van een regressieanalyse wil ik onderzoeken welke factoren binnen het behandeltraject invloed hebben op de wondgenezingstijd en op welke wijze, om op deze manier erachter te komen welke factoren binnen het behandeltraject geoptimaliseerd kunnen worden. In deze analyse moet ik een afweging maken welke variabelen mee te nemen. Naast de informatie vanuit de literatuur wil ik de keuzes voor het meenemen van bepaalde variabelen in de analyse ook onderbouwen met uw mening.

Ik zou graag van u willen weten welke variabelen volgens u de meeste invloed hebben op de wondgenezingtijd. Ik vraag u om de 5 belangrijkste variabelen te selecteren uit onderstaande lijst en deze te rangschikken van 1 tot 5 (van meest belangrijk naar minst belangrijk). Daarnaast vraag ik u om met behulp van het Cardiology grading system uw antwoord te motiveren. Kijkend naar of de 5 variabelen wel of geen invloed hebben op de wondgenezingstijd (I,II,III), en of dit antwoord berust op bewijs uit de literatuur of uw eigen mening (A,B,C).

Alvast bedankt voor uw medewerking.

I. Hey

Prof. dr. R. Geelkerken

MSc. B. Wermelink

Lijst met variabelen:

	Leeftijd		Rutherford Classificatie
	Geslacht		E/A start
	Risico profiel(RP): roken		Type wond
	RP: Cardiaal		Richting wond(Rechts/Links)
	RP: hyperlipidemie		Locatie wond
	RP: Cerebrovasculair		Amputatie risico(WIFI)
	RP: Diabetes		Revascularisatie voordeel(WIFI)
	Diabetes type		Tijd tussen bepalen beleid en uitvoeren Beleid
	BMI		Operatie: Locatie
	VAS score		Operatie: Open
	Doorverwijzing door		Operatie: Extra
	Toegangstijd		Operatie: Duur
	Specialisten tijdens intake		Vaatchirurgen tijdens operatie
	Aanvullend onderzoek		Anesthesioloog
	Eerdere terugkomst		Aantal assistenten
	Intake consulten		Soort anesthesiologie
	Consulten voor OK		Complicaties
	Consulten na OK		Clavien dindo classificatie
	Telefoon consulten		Ziekenhuisdagen
	Gips consulten		
	Aantal MDO's		

Aanbevelingen	
I	Bewijs en of algemene overeenstemming dat deze factor invloed heeft of de wondgenezingstijd
II	Tegenstrijdig bewijs en of een meningsverschil over of deze factor invloed heeft op de wondgenezing
III	Bewijs of algemene overeenstemming dat deze factor geen invloed heeft op de wondgenezingstijd

Bewijs	
Antwoord afkomstig van meerdere gerandomiseerde klinische onderzoeken of meta-analyses	A
Antwoord afkomstig van een enkele gerandomiseerde klinische studie of grote niet-gerandomiseerde studies	B
Antwoord vanuit mening van de experts en of kleine studies retrospectieve studies	C

Antwoord:

	Variabele	Aanbeveling (I, II, III)	Bewijs (A, B of C)
1	Tijd tussen bepalen beleid en uitvoeren Beleid	I	C
2	Toegangstijd	I	B
3	Revascularisatie voordeel(WIFI)	I	C
4	RP: Diabetes	I	C
5	Risico profiel(RP): roken	I	C

Appendix E Socio-Demographics

Socio demographics: Risk profile, wound specifications

Variable	Unit	Frequency	Percent	Variable	Unit	Frequency 1	Percent 1	Frequency 2	Percent 2
Gender	Male	91	67,4%	**Wound existence**	0-3 weeks	64	47,4%		
	Female	44	32,6%		4-8 weeks	49	39,3%		
Age	40-59 year	10	7,4%		More than 8 weeks	22	16,3%		
	60-79 year	78	57,8%	**Number of wounds**	1 wound	90	66,6%		
	80-99 year	47	34,8%		2 wounds	45	33,3%		
	Mean (SD)	75 (9,851)		**Wound type**	Arterial ulcer	67	49,6%	18	40,0%
BMI	Underweight	9	6,7%		Diabetic ulcer + arterial problem	48	35,6%	15	33,3%
	Normalweight	35	25,9%		Other + arterial problem	20	14,8%	12	26,7%
	Overweight	57	42,2%	**Wound direction**	Right	77	57%	21	46,7%
	Obesity	34	25,2%		Left	58	43%	24	53,3%
Smoking	No	45	33,3%	**Wound location**	Dig 1	44	32,6%	11	24,4%
	Yes	85	63,0%		Dig 2-5	47	34,8%	18	40,0%
	Missing value	5	3,7%		Interdigit, forefoot, Plantar and lateral edge	17	12,6%	6	13,3%
Cardial Risk	No	54	40,0%		Lower leg, Ankle, Heel Calf	27	20,0%	10	22,2%
	Myocardial infraction	24	17,8%	**Amputation risk**	Stage 1	38	28,1%	15	33,3%
	Other	55	40,7%		Stage 2	43	31,9%	13	28,9%
	Missing value	2	1,5%		Stage 3	40	29,6%	15	33,3%
Hyperlipidemia	No	44	32,6%		Stage 4	14	10,4%	2	4,4%
	Yes	83	61,5%	**Revascularization benefit**	Stage 1	60	44,1%	21	46,7%
	Missing value	8	5,9%		Stage 2	10	7,4%	2	4,4%
Cerebrovascular	No	107	79,3%		Stage 3	28	20,7%	10	22,2%
	TIA	13	9,6%		Stage 4	37	27,4%	12	26,7%
	CVA	13	9,6%	**Rutherford classification**	R1-3	5 (R)	3,7%	3 (L)	2,2%
	Missing value	2	1,5%		R4	0 (R)	0,0%	1 (L)	0,7%
Diabetic	Yes	89	65,9%		R5	73 (R)	54,1%	58 (L)	43,0%
	No	46	34,1%		R6	4 (R)	3,0%	1 (L)	0,7%
Diabetic type	Type 1	4			Other	0 (R)	0,0%	1 (L)	0,7%
	Type 2	85							

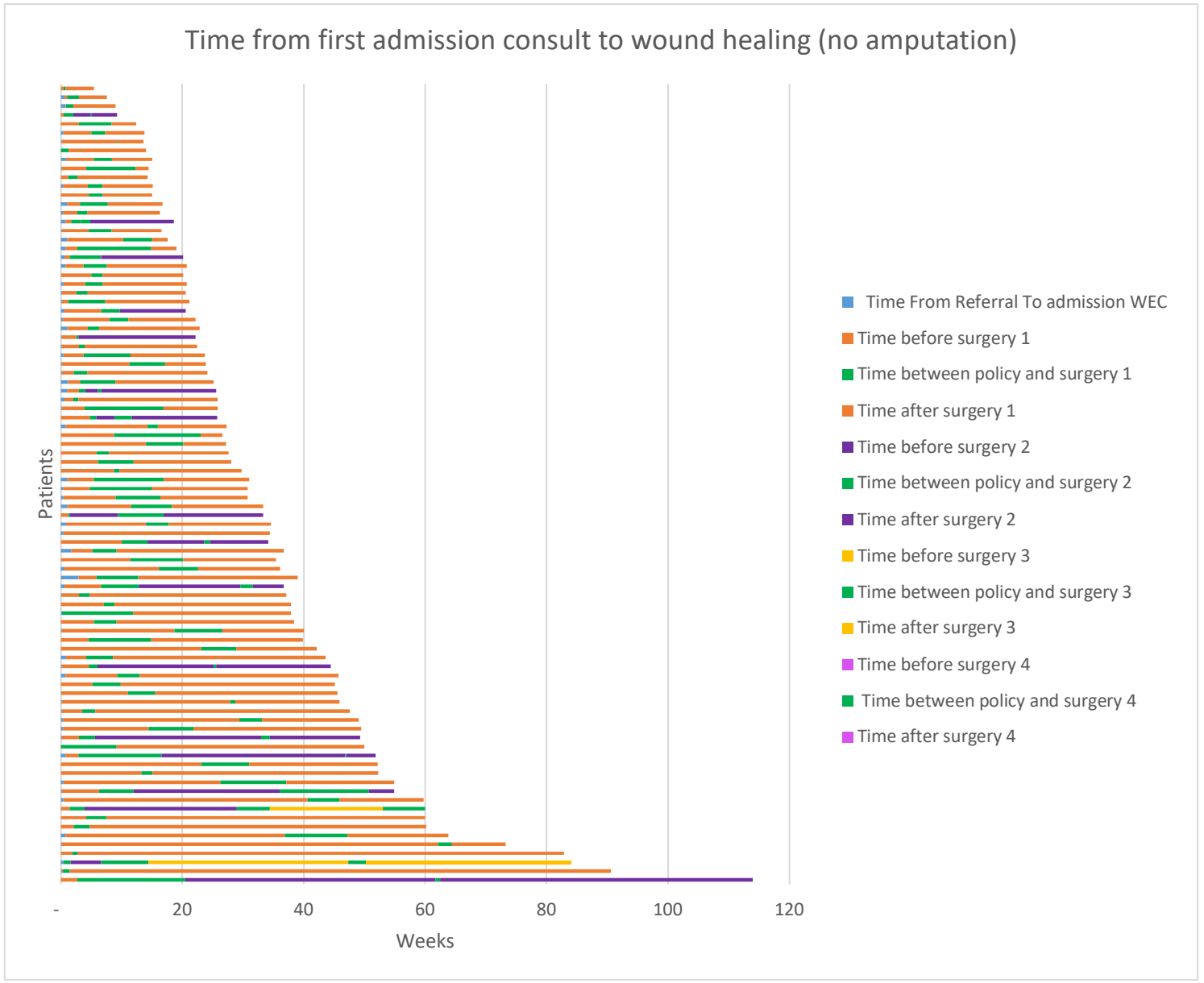
Socio demographics: treatment process

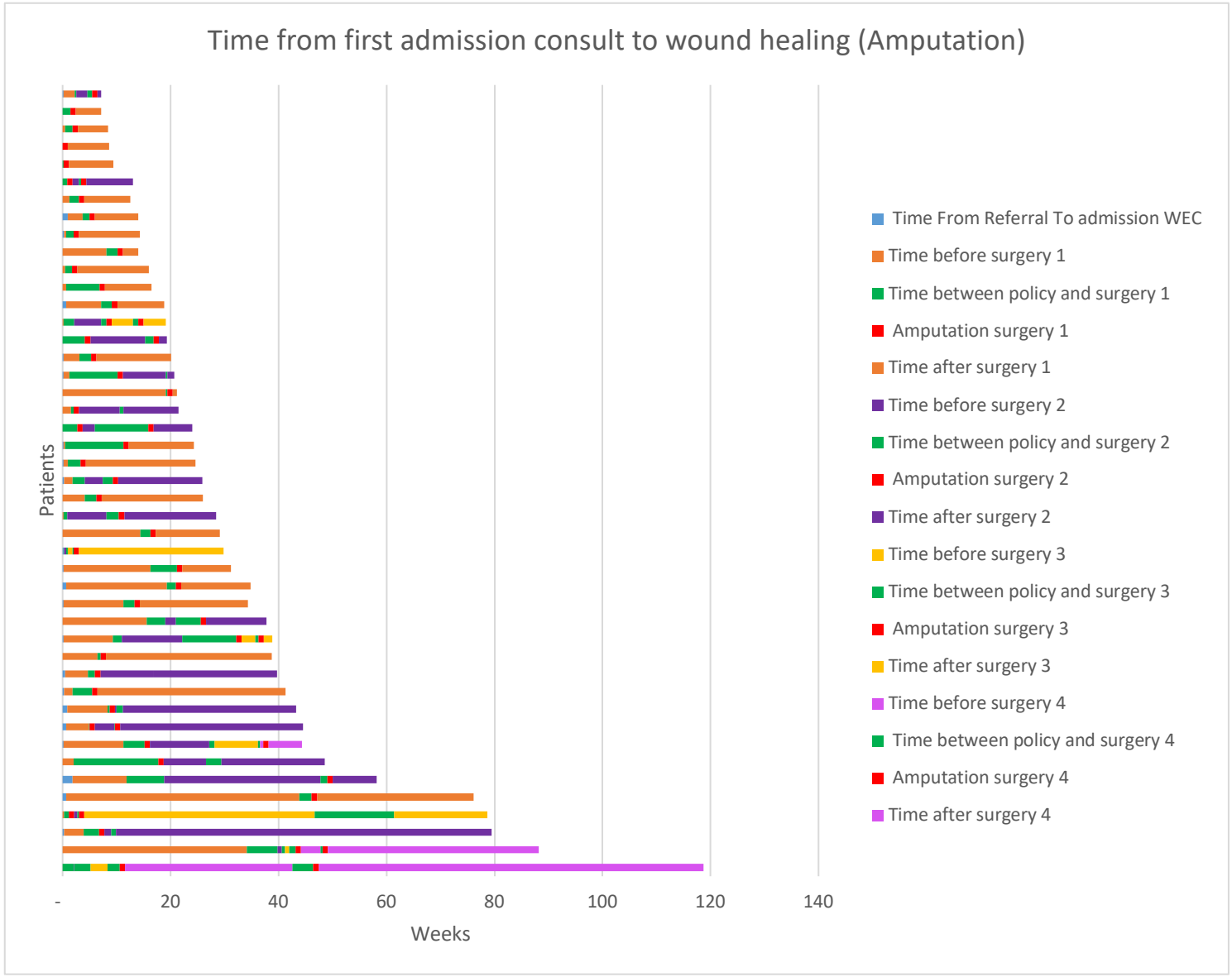
Variable	Unit	Frequency	Percent	Variable	Unit	Frequency	Percent
Referral by	Within MST	21	15,6%	**Control consults after surgery 1**	0-2 consults	37	27,4%
	General Practitioner	100	74,1%		3-5 consults	35	25,9%
	Other	14	10,4%		6-8 consults	32	23,7%
Time from referral to admission WEC	0-2 days	62	45,9%		More than 8 consults	31	23,0%
	3-5 days	28	20,7%	**Control consults after surgery 3**	0-2 consults	13	33,3%
	More than 5 days	15	11,1%		3-5 consults	12	30,8%
	Unknown	30	22,2%		6-8 consults	5	12,8%
Specialist during admission	Vascular + Nurse	96	71,1%		More than 8 consults	9	23,1%
	Vascular + Nurse + Podotherapist or Revalidation specialist	17	12,6%	**Control consults after surgery 3/4**	0-2 consults	4	44,4%
	Other	22	16,3%		3-5 consults	1	11,1%
Additional examination	CTA + extra	33	24,4%		6-8 consults	2	22,2%
	MRA + extra	53	39,3%		More than 8 consults	2	22,2%
	Other	49	36,3%	**Phone consults**	0-2 consults	91	67,4%
Earlier Return	No	84	62,2%		3-5 consults	26	19,3%
	1 time	35	25,9%		More than 5 consults	18	13,3%
	More than 1 time	16	11,9%	**Gypsum consult**	No	104	77,0%
Admission consults	1 admission	126	93,3%		Yes	31	23,0%
	More than 1 admission	9	6,7%	**MDO's**	None	11	8,1%
Control consults before surgery	0-2 consults	56	41,5%		1 MDO	86	63,7%
	3-5 consults	38	28,1%		2 MDO's	23	17,0%
	6-8 consults	23	17,0%		More than 2 MDO's	15	11,1%
	More than 8 consults	18	13,3%				

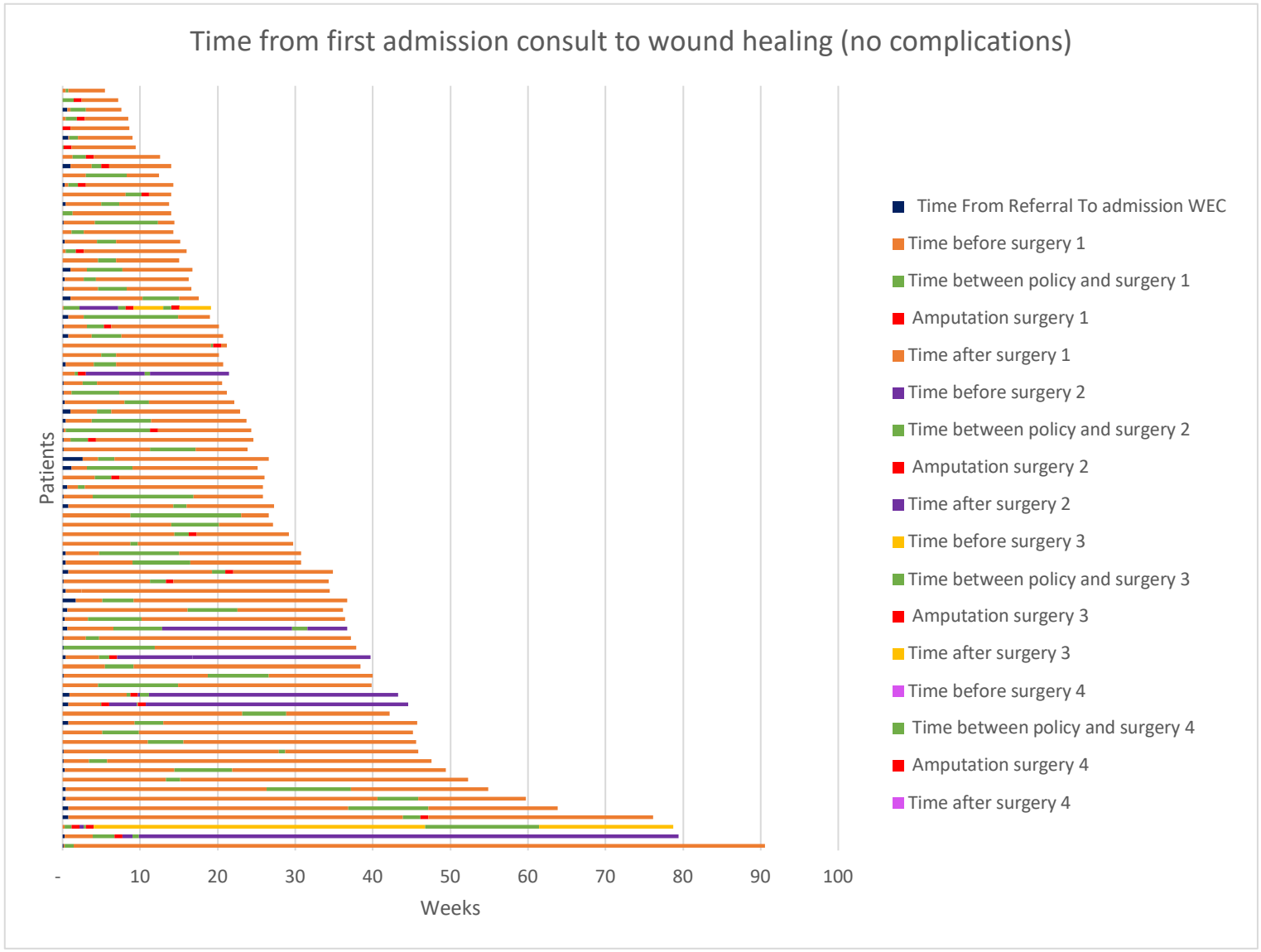
Socio demographics: Surgery specifications

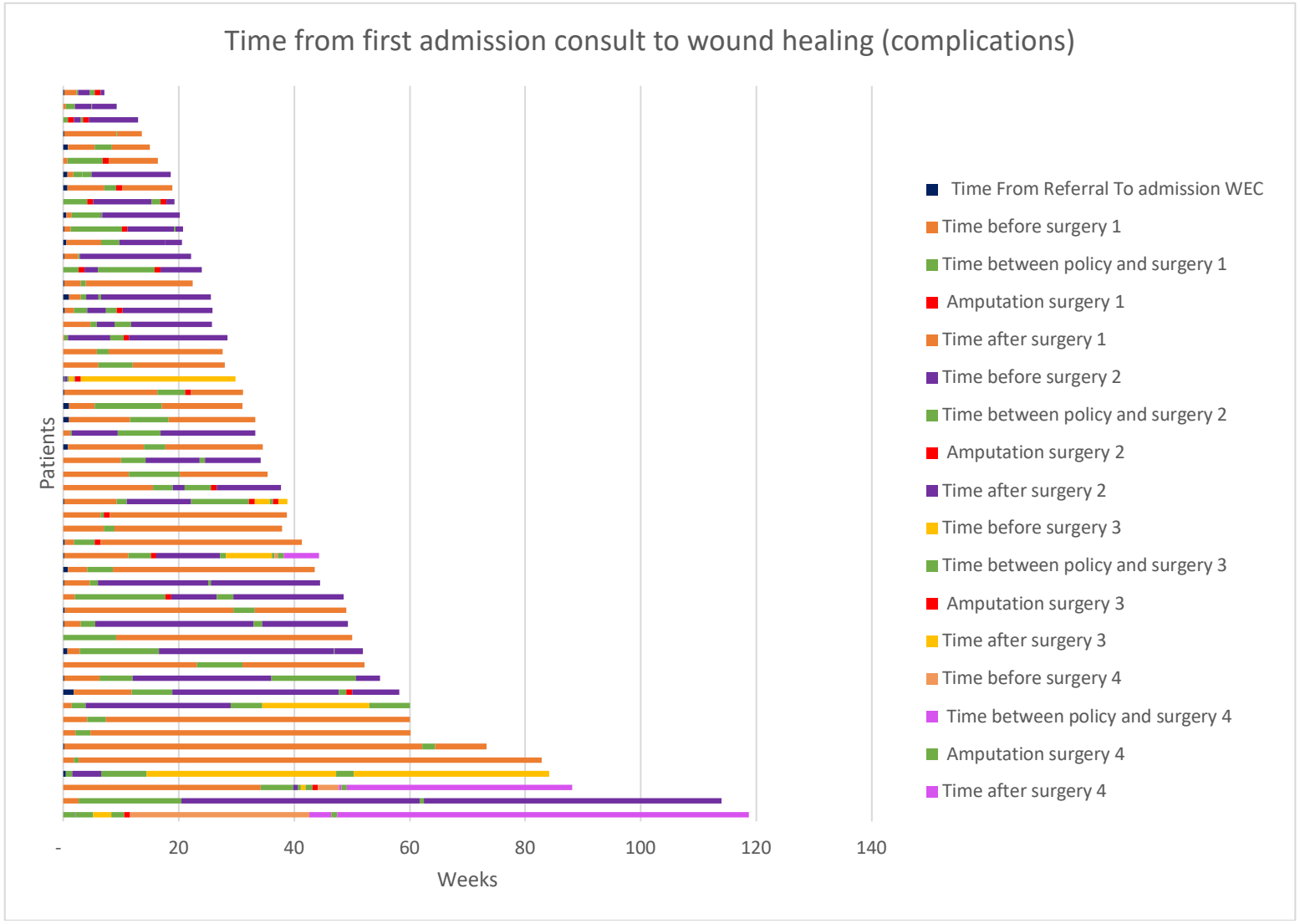
Variable	Unit	Frequency 1	Percent 1	Variable	Unit	Frequency 1	Percent 1	Percent 2	Percent 3	Percent 4
Number of surgeries	1 surgery	96	71,1%	**Clavien dindo classification**	None	73	54,1%			
	2 surgeries	30	22,2%		No need for pharmacological treatment. No deviation from the normal course.	11	8,1%			
	3 surgeries	6	4,4%		Requiring pharmacological treatment (antibiotics)	14	10,4%			
	4 surgeries	3	2,2%		Requiring surgical endoscopic or radiological intervention.	37	27,4%			
Time between policy and surgery	0-2 weeks	69	51,1%	**Length of hospital stay**	1-3 days	46	34,1%			
	3-5 weeks	31	23,0%		4-6 days	25	18,5%			
	6-8 weeks	19	14,1%		7-10 days	24	17,8%			
	More than 8 weeks	16	11,9%		More than 10 days	40	29,6%			
Vascular surgeon 1	Geelkerken	12	8,9%	**Location surgery**	No	17	12,6%	52,5%	66,7%	100,0%
	Meerwaldt	40	29,6%		One level	11	8,1%	7,5%	0,0%	0,0%
	Beuk	29	21,5%		Multilevel	107	79,3%	40,0%	33,3%	0,0%
	Willigendeal	39	28,9%	**Open surgery**	No	82	60,7%	84,6%	88,9%	100,0%
	Surgeon resident	14	10,4%		Bypass	12	8,9%	12,8%	11,1%	0,0%
Vascular surgeon 2	Geelkerken	1	0,7%		Fem-Fem cross over	2	1,5%	0,0%	0,0%	0,0%
	Meerwaldt	8	5,9%		Desobstruction	31	23,0%	2,6%	0,0%	0,0%
	Beuk	3	2,2%		Other	8	5,9%	0,0%	0,0%	0,0%
	Willigendeal	3	2,2%	**Additional surgery**	No	62	45,9%	33,3%	22,2%	0,0%
	Surgeon resident	17	12,6%		Wound toilet	22	16,3%	7,7%	11,1%	0,0%
Number of assistents	0 assistants	74	54,8%		Amputation (s)	37	27,4%	41,0%	55,6%	66,7%
	1 assistant	53	39,3%		Other	14	10,4%	17,9%	11,1%	33,3%
	2 assistants	8	5,9%	**Amputations**	None	90	66,7%			
Kind of anesthesia	ITN	91	67,4%		1 amputation	35	25,9%			
	Balanced	28	20,7%		2 amputations	10	7,4%			
	Other	16	11,9%	**Amputation**	Minor	37	27,4%			
Complications	None	73	54,1%		Major	16	11,9%			
	Occlusion	6	4,4%							
	Infection	20	14,8%							
	No healing	20	14,8%							
	Other	16	11,9%							

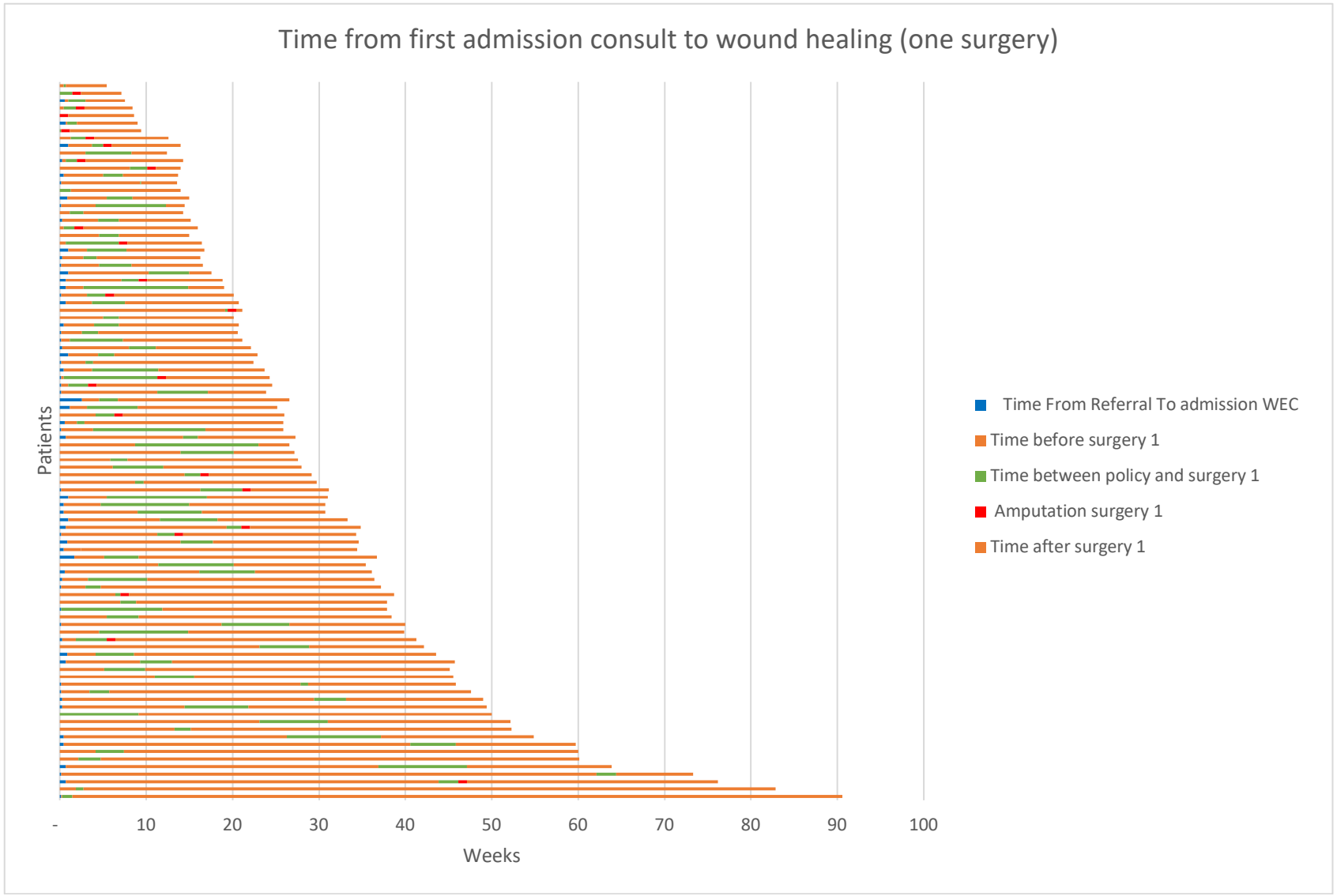
Appendix F. Visualizations of time from first admission consult to wound healing

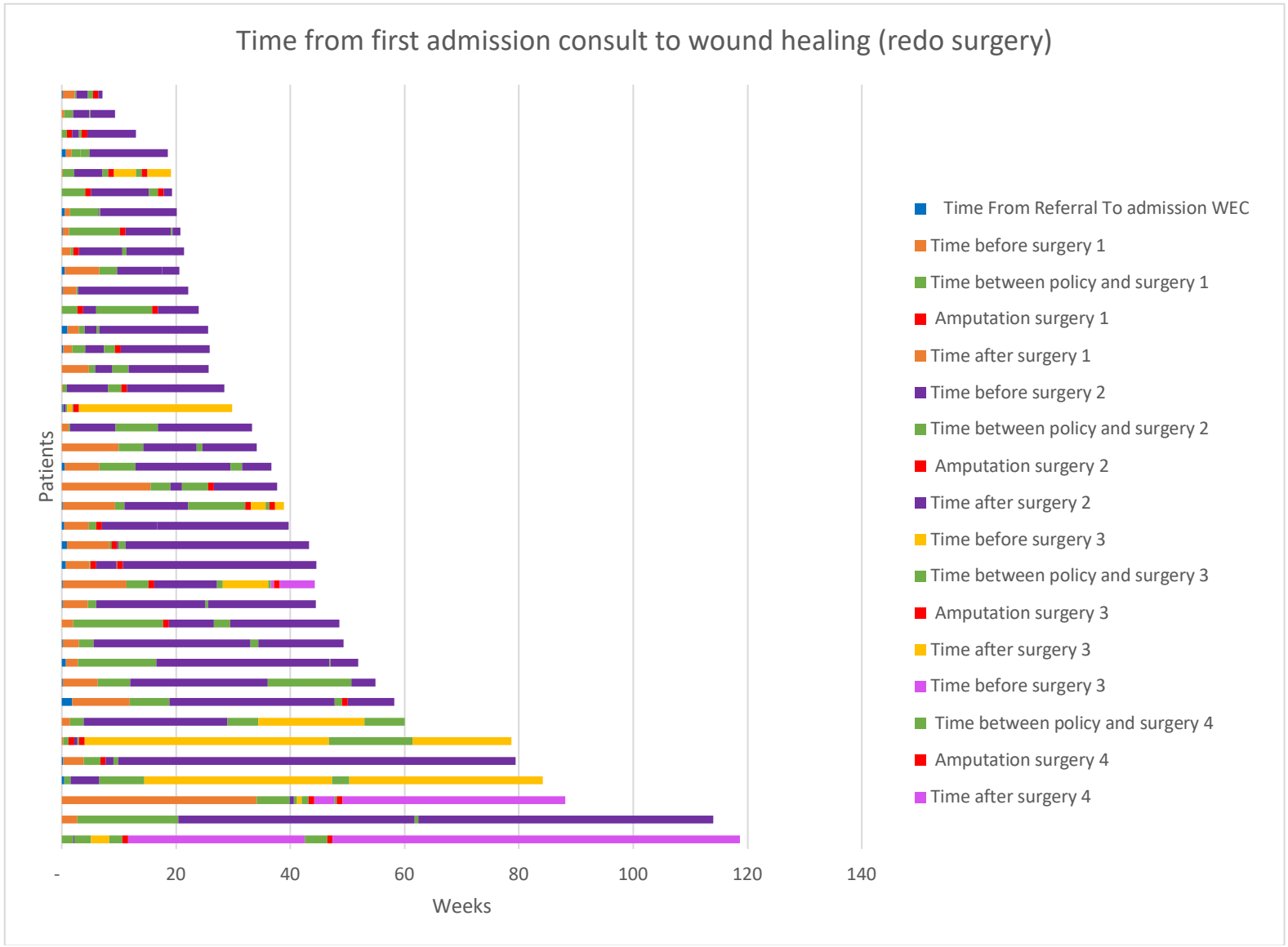



Time from first admission consult to wound healing (Amputation)
Patients
Weeks
-
20
40
60
80
100
120
140
Time From Referral To admission WEC
Time before surgery 1
Time between policy and surgery 1
Amputation surgery 1
Time after surgery 1
Time before surgery 2
Time between policy and surgery 2
Amputation surgery 2
Time after surgery 2
Time before surgery 3
Time between policy and surgery 3
Amputation surgery 3
Time after surgery 3
Time before surgery 4
Time between policy and surgery 4
Amputation surgery 4
Time after surgery 4


Time from first admission consult to wound healing (no complications)
Patients
Weeks
-
10
20
30
40
50
60
70
80
90
100
Time From Referral To admission WEC
Time before surgery 1
Time between policy and surgery 1
Amputation surgery 1
Time after surgery 1
Time before surgery 2
Time between policy and surgery 2
Amputation surgery 2
Time after surgery 2
Time before surgery 3
Time between policy and surgery 3
Amputation surgery 3
Time after surgery 3
Time before surgery 4
Time between policy and surgery 4
Amputation surgery 4
Time after surgery 4


Time from first admission consult to wound healing (complications)
Patients
Weeks
-
20
40
60
80
100
120
140
Time From Referral To admission WEC
Time before surgery 1
Time between policy and surgery 1
Amputation surgery 1
Time after surgery 1
Time before surgery 2
Time between policy and surgery 2
Amputation surgery 2
Time after surgery 2
Time before surgery 3
Time between policy and surgery 3
Amputation surgery 3
Time after surgery 3
Time before surgery 4
Time between policy and surgery 4
Amputation surgery 4
Time after surgery 4

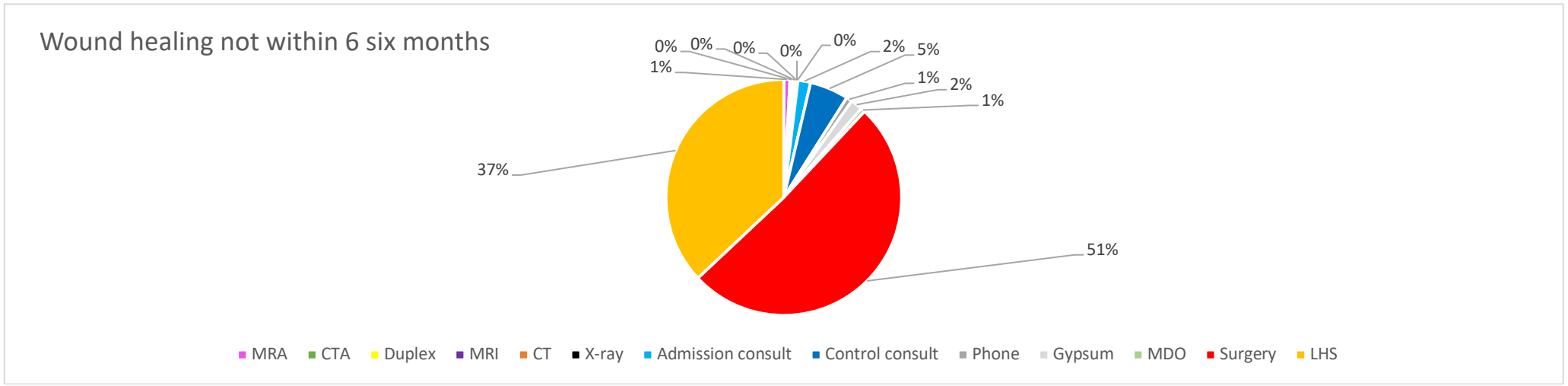

Time from first admission consult to wound healing (one surgery)
Patients
Weeks
-
10
20
30
40
50
60
70
80
90
100
Time From Referral To admission WEC
Time before surgery 1
Time between policy and surgery 1
Amputation surgery 1
Time after surgery 1

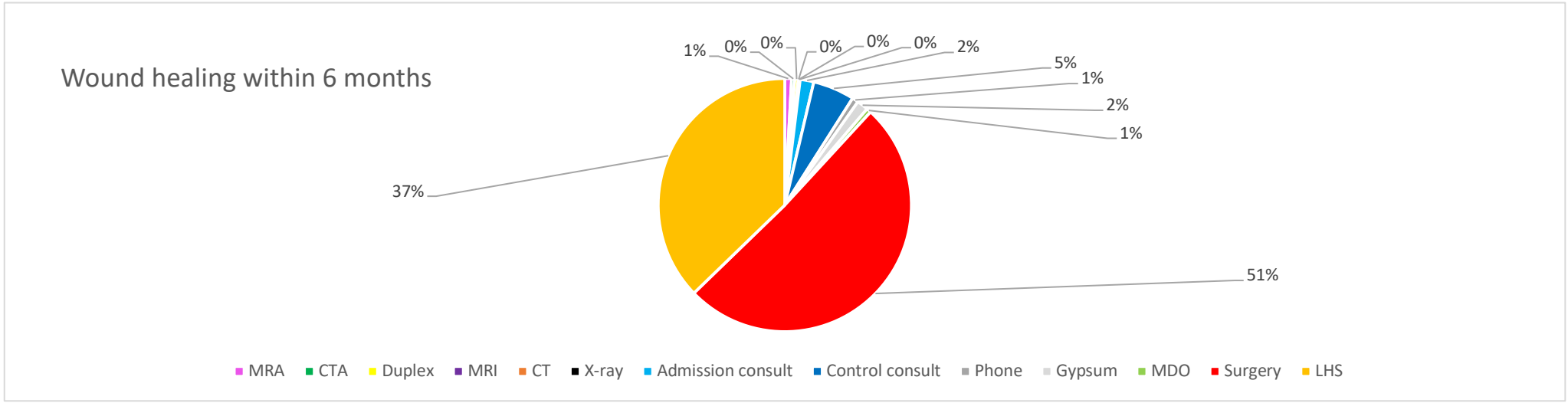

Time from first admission consult to wound healing (redo surgery)
Patients
Weeks
-
20
40
60
80
100
120
140
Time From Referral To admission WEC
Time before surgery 1
Time between policy and surgery 1
Amputation surgery 1
Time after surgery 1
Time before surgery 2
Time between policy and surgery 2
Amputation surgery 2
Time after surgery 2
Time before surgery 3
Time between policy and surgery 3
Amputation surgery 3
Time after surgery 3
Time before surgery 3
Time between policy and surgery 4
Amputation surgery 4
Time after surgery 4

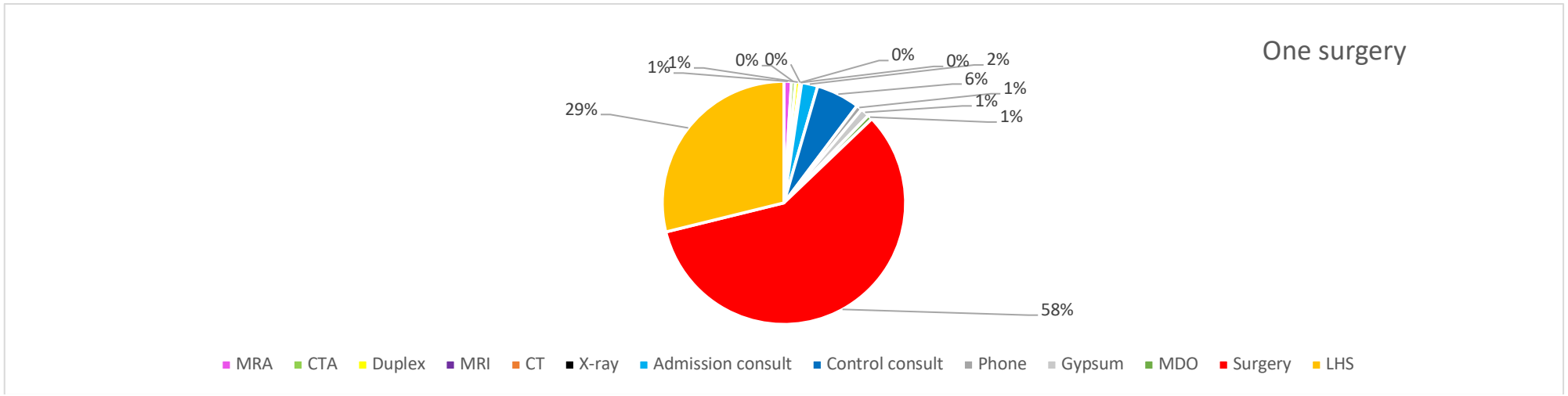
Appendix G **ANOVA test/ Welch test**

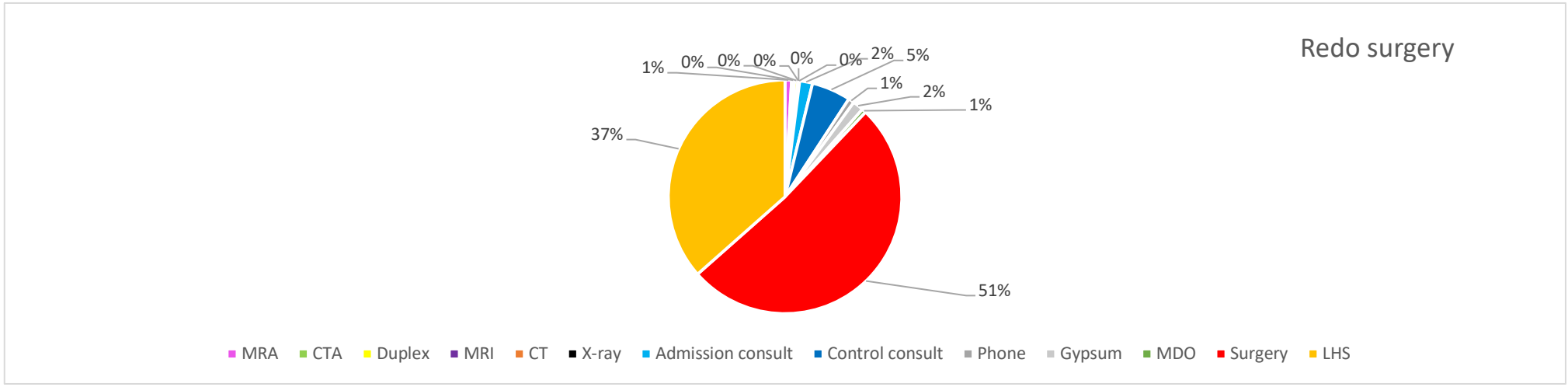
Factor	*Anova*	*Welch*
Cerebrovascular risk		0,048**
Referral By		0,122**
Additional examination		0,153**
Specialists at admission	0,835	
Wound location		0,457
Amputation risk		0,372
Revascularization benefit	0,728	
Open surgery	0,946	
Additional surgery	0,000 *	
Kind of Anesthesia		0,515
Clavien-dindo classification		0,013*

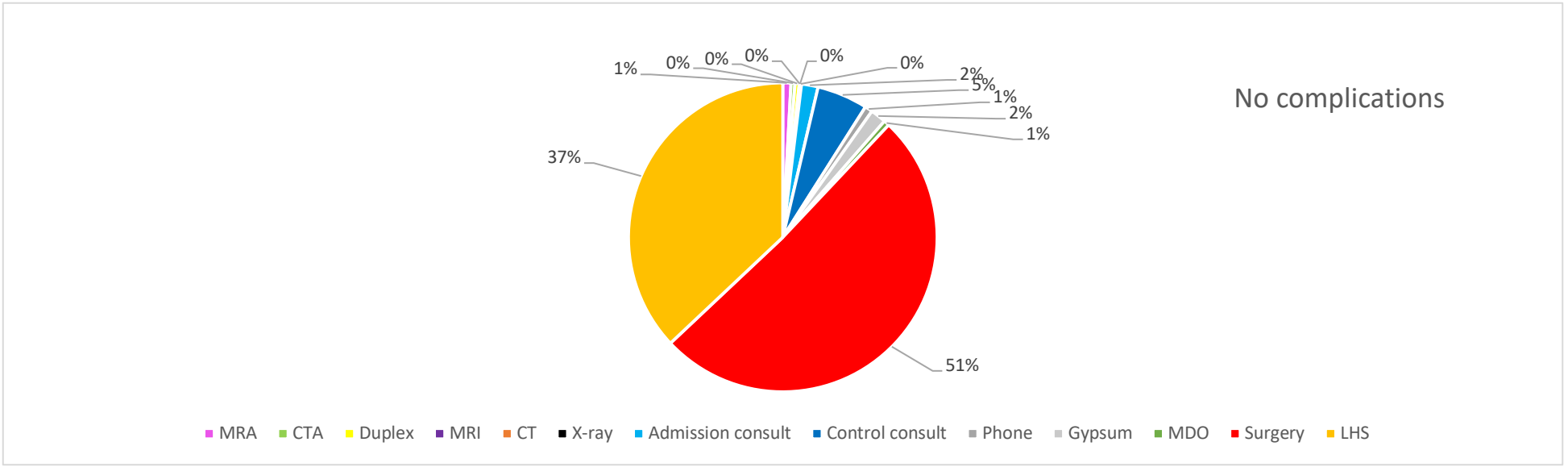
Appendix H.1 Distribution of costs for the wound healing process

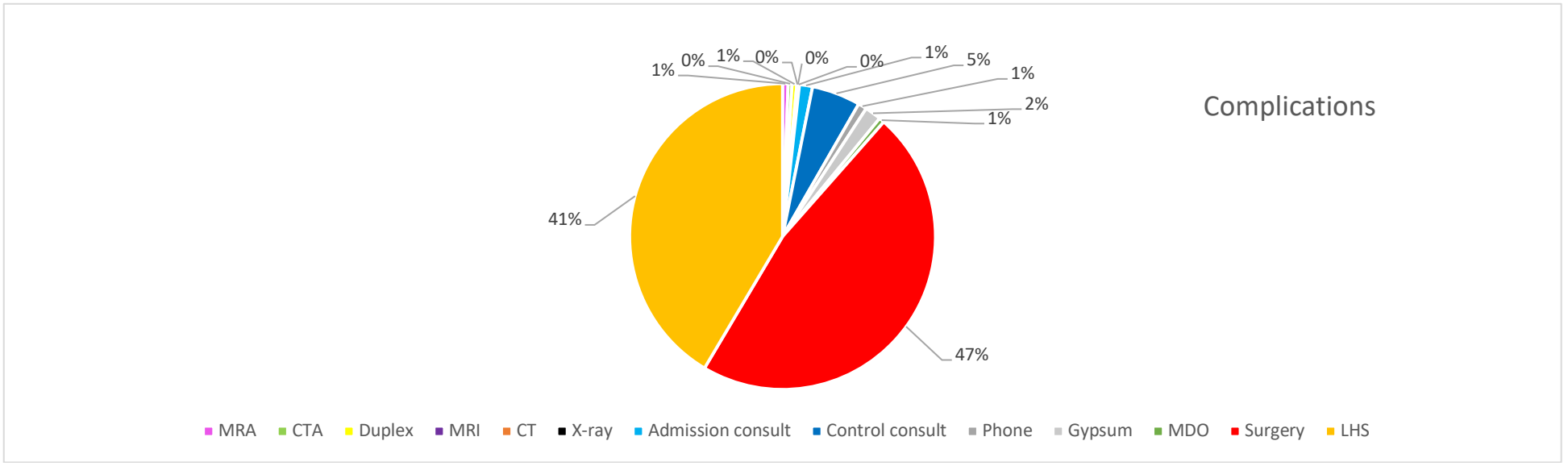


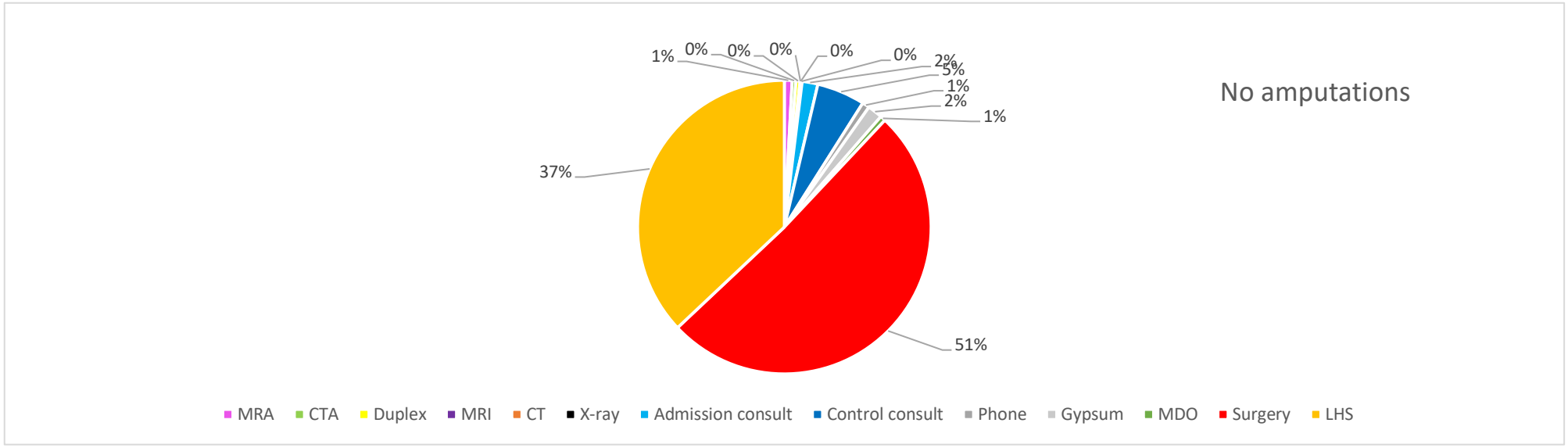


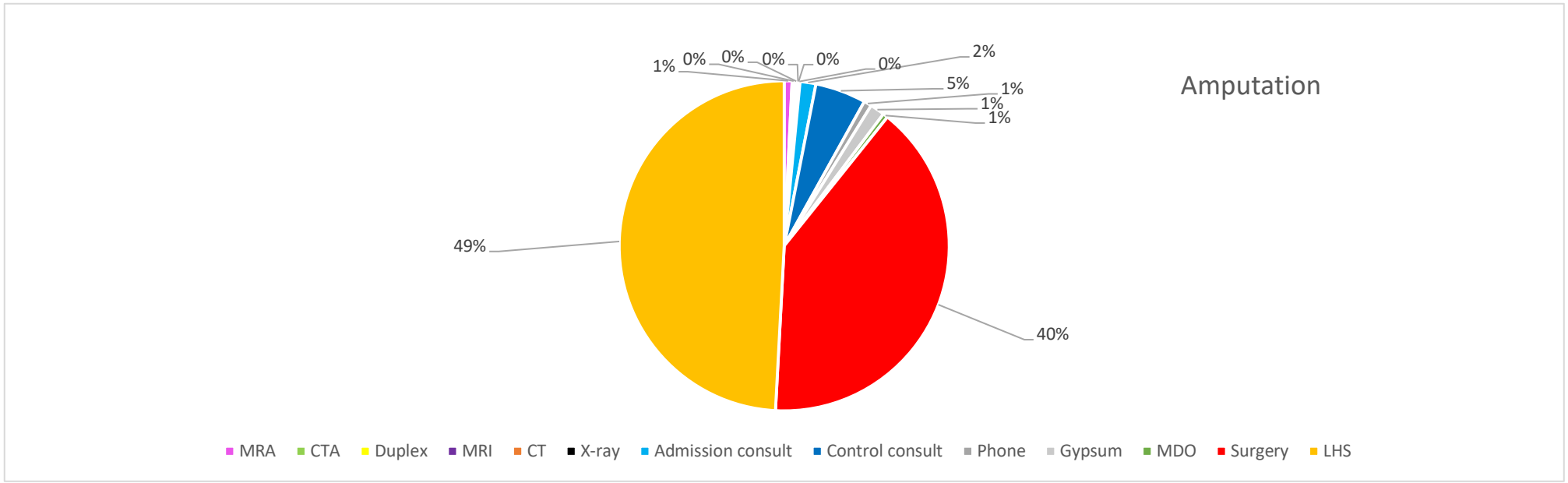

One surgery
1%
1%
0%
0%
0%
0%
2%
6%
1%
1%
1%
29%
58%
MRA
CTA
Duplex
MRI
CT
X-ray
Admission consult
Control consult
Phone
Gypsum
MDO
Surgery
LHS


Redo surgery
1%
0%
0%
0%
0%
0%
2%
5%
1%
2%
1%
37%
51%
MRA
CTA
Duplex
MRI
CT
X-ray
Admission consult
Control consult
Phone
Gypsum
MDO
Surgery
LHS

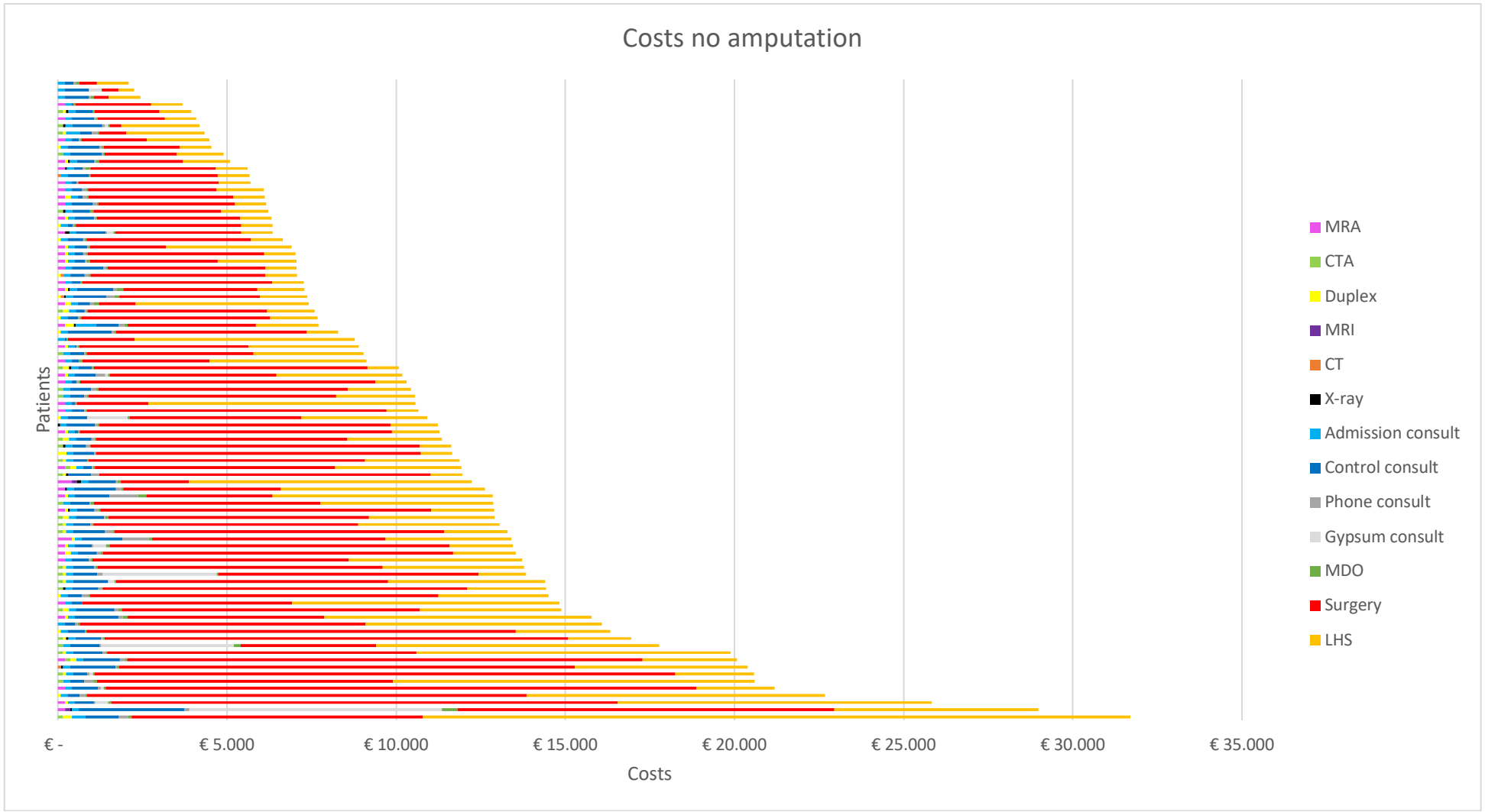

No complications
1%
0%
0%
0%
0%
0%
2%
5%
1%
2%
1%
37%
51%
MRA
CTA
Duplex
MRI
CT
X-ray
Admission consult
Control consult
Phone
Gypsum
MDO
Surgery
LHS

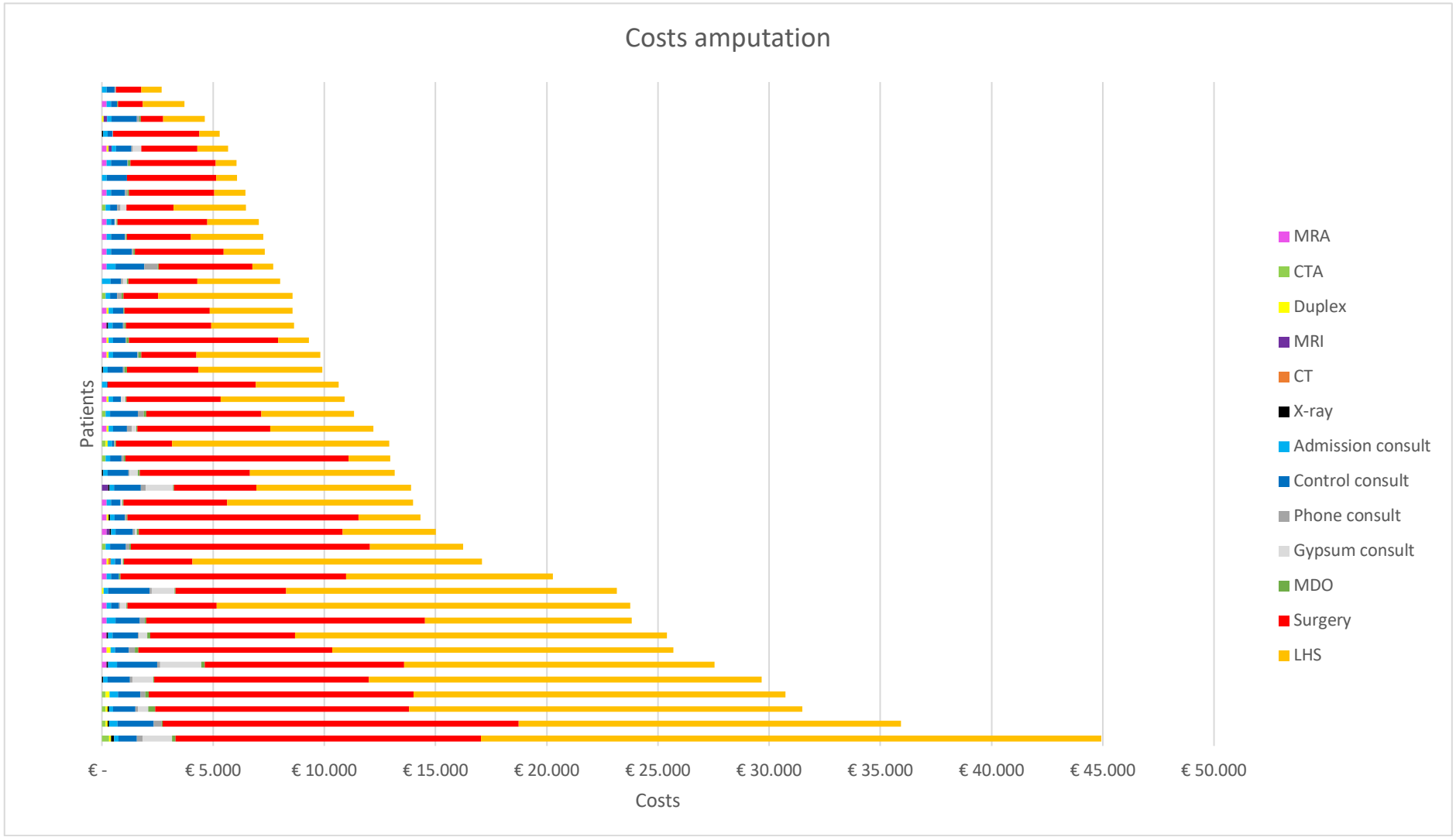

Complications
1%
0%
1%
0%
0%
0%
1%
5%
1%
2%
1%
41%
47%
MRA
CTA
Duplex
MRI
CT
X-ray
Admission consult
Control consult
Phone
Gypsum
MDO
Surgery
LHS

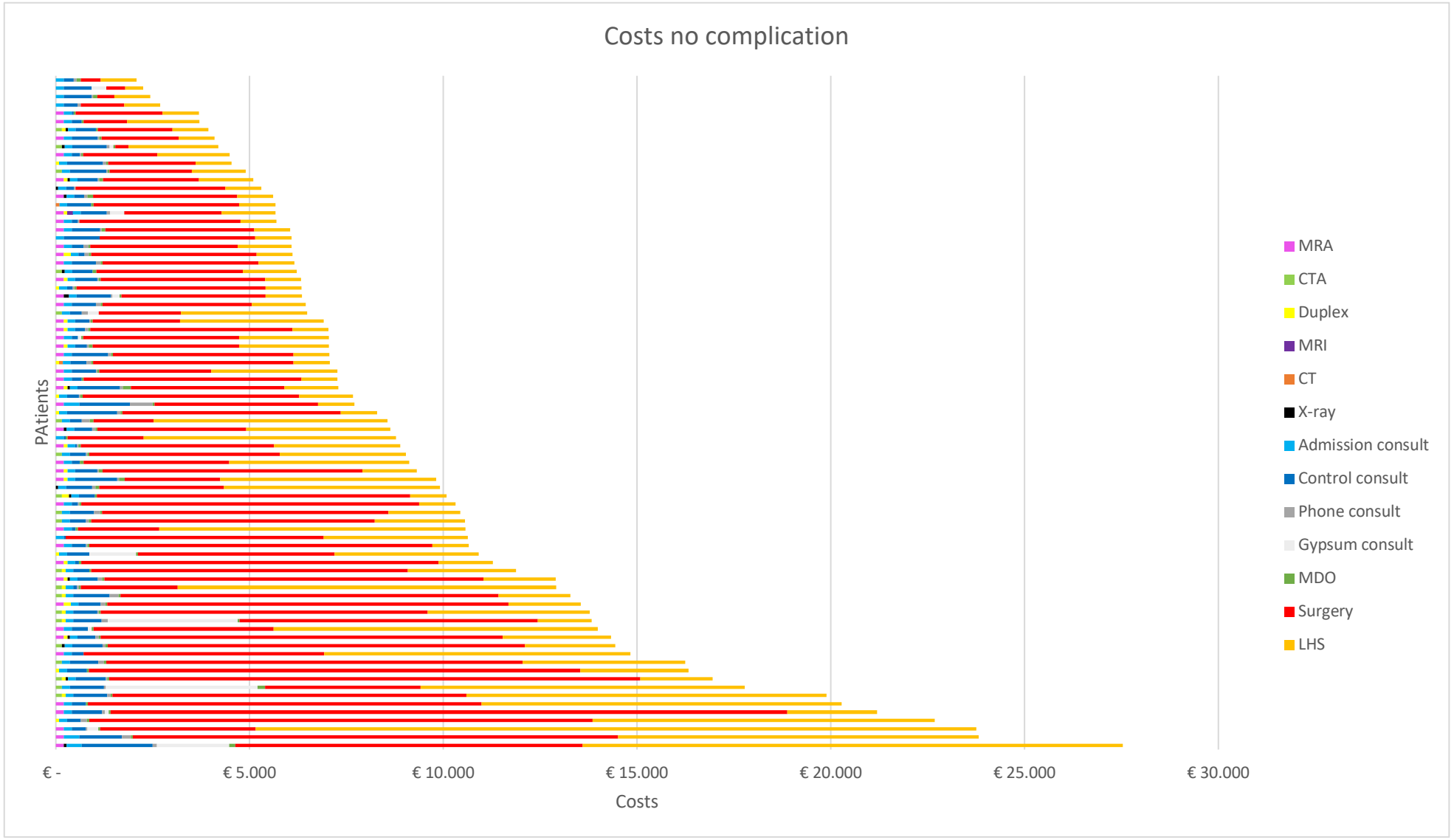

No amputations
1%
0%
0%
0%
0%
0%
2%
5%
1%
2%
1%
37%
51%
MRA
CTA
Duplex
MRI
CT
X-ray
Admission consult
Control consult
Phone
Gypsum
MDO
Surgery
LHS

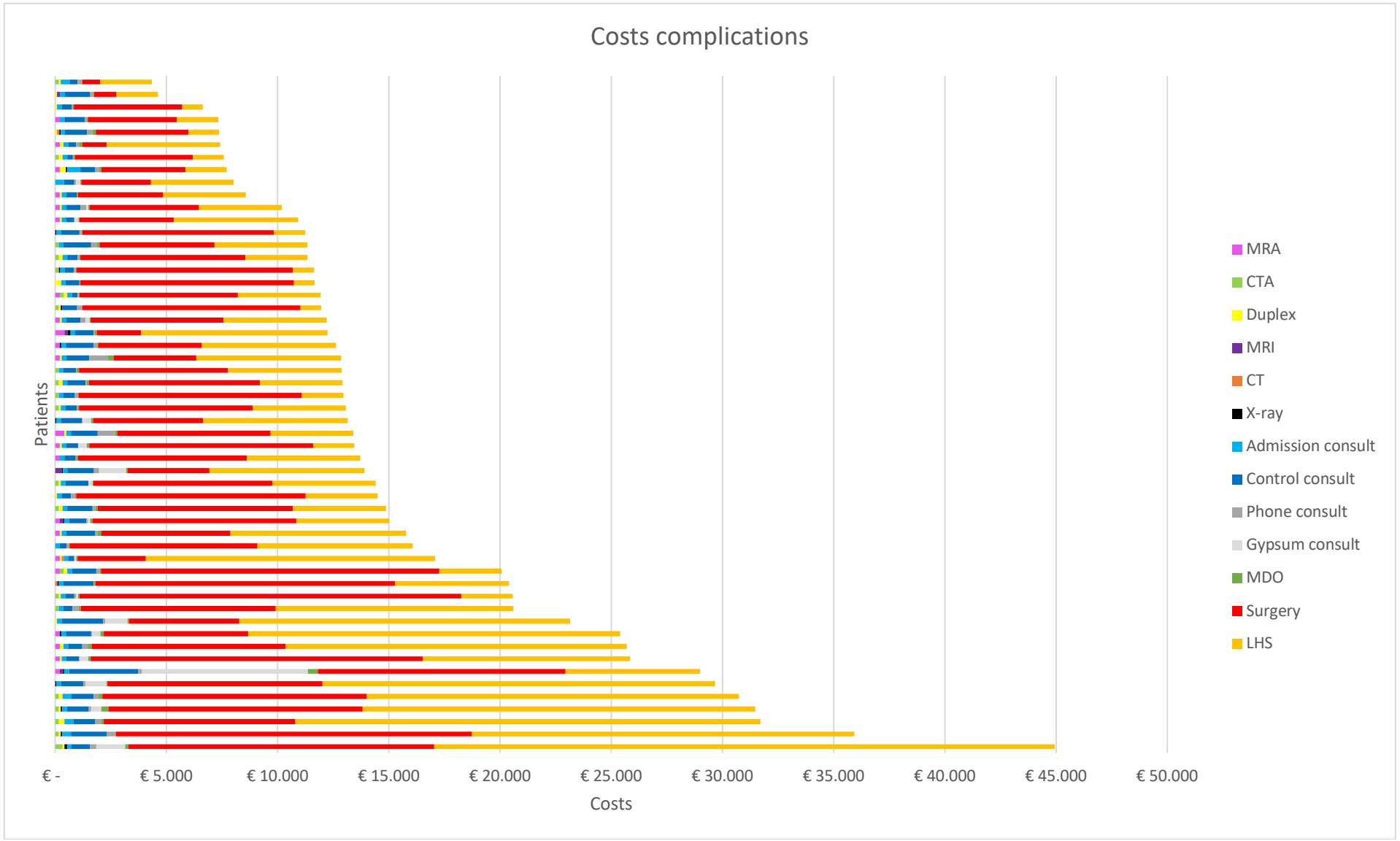

Amputation
1%
0%
0%
0%
0%
0%
2%
5%
1%
1%
1%
49%
40%
MRA
CTA
Duplex
MRI
CT
X-ray
Admission consult
Control consult
Phone
Gypsum
MDO
Surgery
LHS

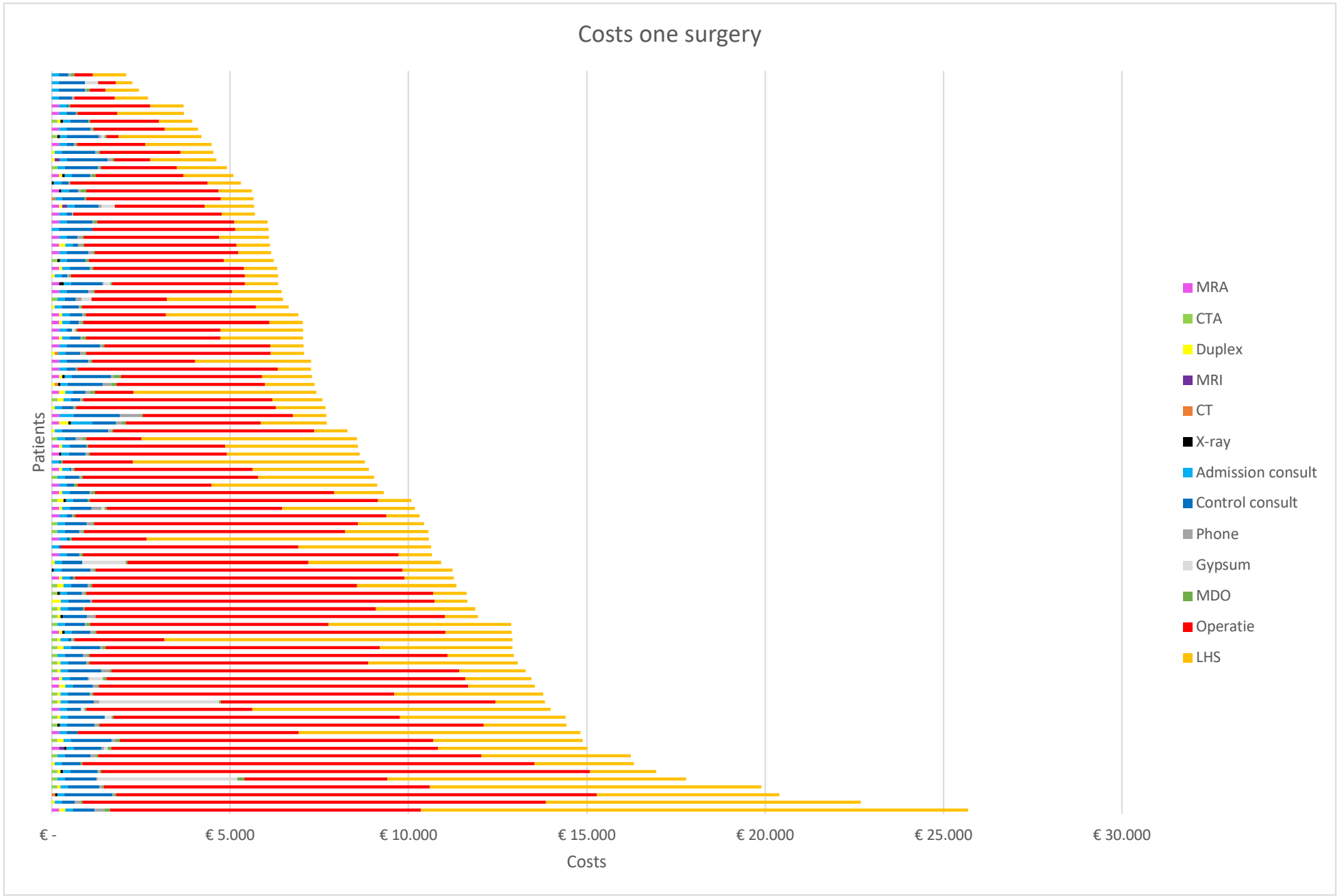
Appendix H.2 Visualization of time from first admission consult to wound healing based on costs

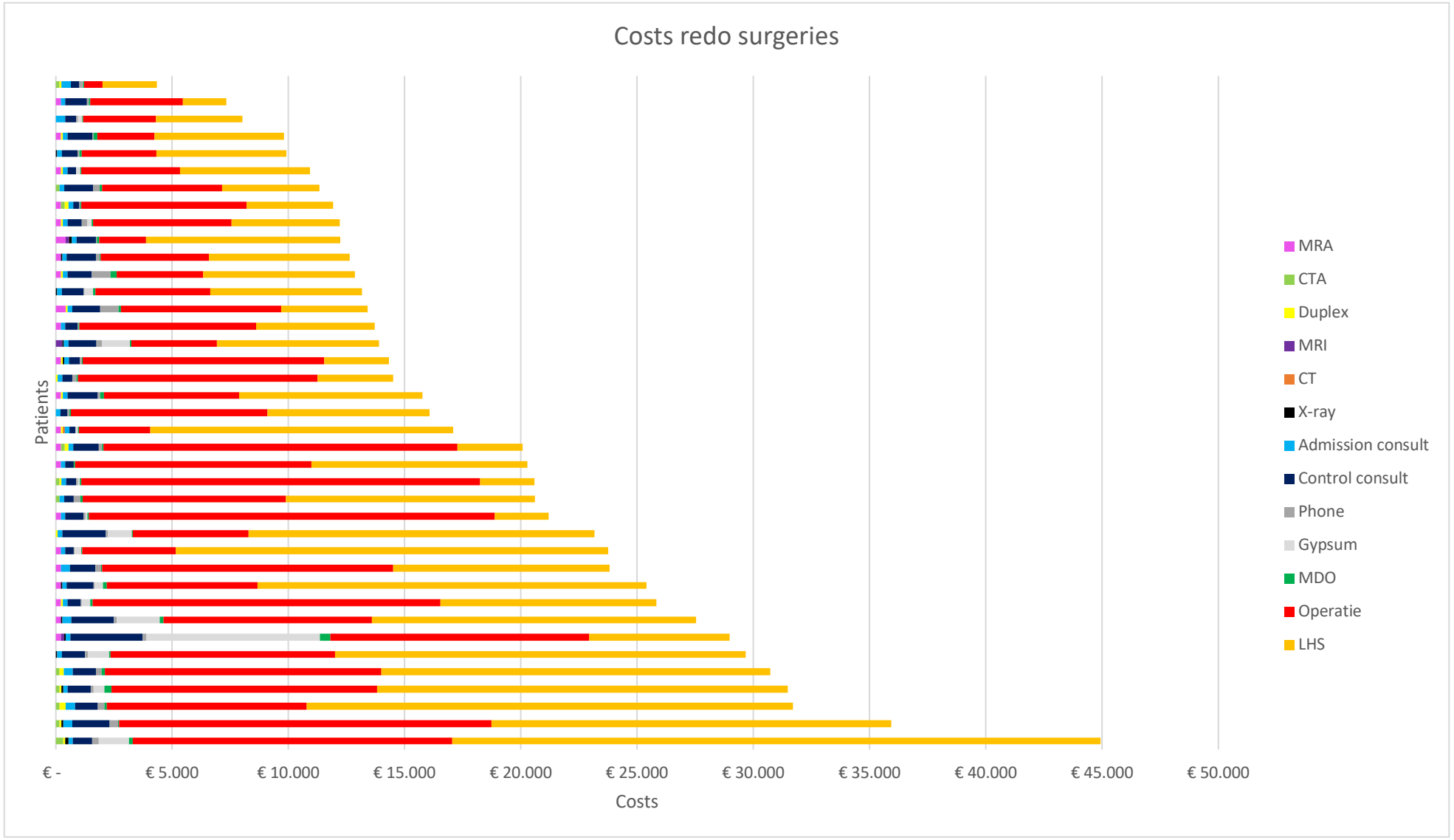



Costs amputation
Patients
€ -
€ 5.000
€ 10.000
€ 15.000
€ 20.000
€ 25.000
€ 30.000
€ 35.000
€ 40.000
€ 45.000
€ 50.000
Costs
MRA
CTA
Duplex
MRI
CT
X-ray
Admission consult
Control consult
Phone consult
Gypsum consult
MDO
Surgery
LHS


Costs no complication
PAtients
€ -
€ 5.000
€ 10.000
€ 15.000
€ 20.000
€ 25.000
€ 30.000
Costs
MRA
CTA
Duplex
MRI
CT
X-ray
Admission consult
Control consult
Phone consult
Gypsum consult
MDO
Surgery
LHS


Costs complications
Patients
€ -
€ 5.000
€ 10.000
€ 15.000
€ 20.000
€ 25.000
€ 30.000
€ 35.000
€ 40.000
€ 45.000
€ 50.000
Costs
MRA
CTA
Duplex
MRI
CT
X-ray
Admission consult
Control consult
Phone consult
Gypsum consult
MDO
Surgery
LHS


Costs one surgery
Patients
€ -
€ 5.000
€ 10.000
€ 15.000
€ 20.000
€ 25.000
€ 30.000
Costs
MRA
CTA
Duplex
MRI
CT
X-ray
Admission consult
Control consult
Phone
Gypsum
MDO
Operatie
LHS


Costs redo surgeries
Patients
Costs
€ -
€ 5.000
€ 10.000
€ 15.000
€ 20.000
€ 25.000
€ 30.000
€ 35.000
€ 40.000
€ 45.000
€ 50.000
MRA
CTA
Duplex
MRI
CT
X-ray
Admission consult
Control consult
Phone
Gypsum
MDO
Operatie
LHS